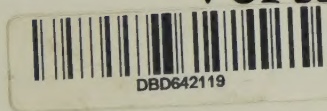


The
Segmentation Of The Nervous
System In *Squalus Acanthias*:
A Contribution To The
Morphology Of The
Vertebrate Head
(1898)



Herbert Vincent Neal

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THE SEGMENTATION OF THE NERVOUS SYSTEM IN
SQUALUS ACANTHIAS.

A CONTRIBUTION TO THE MORPHOLOGY OF THE
VERTEBRATE HEAD.

By H. V. NEAL.

WITH NINE PLATES.

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NO. 7.—*The Segmentation of the Nervous System in Squalus acanthias. A Contribution to the Morphology of the Vertebrate Head.*¹ By H. V. NEAL.

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¹ Contributions from the Zoological Laboratory of the Museum of Comparative Zoölogy at Harvard College, under the direction of E. L. Mark, No. LXXXIX.

Introduction.

CRITERIA OF SEGMENTATION.

MORPHOLOGISTS have long sought to compare in Vertebrates a head segment with a trunk segment. They have assumed that in the ancestors of Vertebrates head and trunk were differentiated from each other, and that similar segments once extended throughout the entire length of the body. Direct evidence in favor of this assumption is now furnished, it is held, by *Amphioxus*. Because of the many difficulties involved, the problem has become a favorite one, and since the early attempts made by the poet Goethe and anatomists of the "Transcendental" school, many men have contributed evidence and theory in the hope of its solution. Since Goethe and Oken maintained the bony cranium to be composed of fused vertebrae comparable with those in the vertebral column, the problem has passed through several phases. First, Huxley ('58), upon broad comparative anatomical evidence, proved that nothing like a vertebra is to be found in the cranium of either high or low Vertebrates, and he concluded as a result of his researches that morphologists, in attempting to find a primitive metamerism in a structure which is so late in its phylogenetic appearance as the bony cranium, were approaching the problem in the wrong direction. In thus disproving the "vertebral theory" of the Vertebrate cranium, however, "war die Frage doch noch nicht aus der Welt geschafft," as Gegenbaur wrote in his famous "Kritik." By Gegenbaur ('72) the question was transformed into a problem of the phylogenesis of the *entire* head. By using as criteria the visceral arches and the nerves which innervate them, he attempted to determine the number of primitive segments in the head of those low Vertebrates, the Selachii, which in his opinion most resembled the hypothetical Vertebrate ancestors.

With the gradual acceptance of the "fundamental law of biogenesis," that the development of an individual is an epitome of the development of the race, the evidence offered in the solution of the problem of the morphology of the Vertebrate head has become more and more embryological.

After Balfour's ('78) discovery that the primary body cavity of Selachian embryos extends unbroken into the head region, and the further discovery of Marshall ('81) that in these embryos the body cavity of the head undergoes an independent segmentation into mesodermal cavities, Selachian embryos became the chief objects of research. It was finally

left to van Wijhe ('82) to demonstrate in Selachian embryos an uninterrupted continuity, and a direct morphological comparability, of head and trunk "Mesodermsegments," and thus, in the opinion of many morphologists, the existence of an "acraniote" stage in the development of craniote embryos. Since the "mesodermal segments" or somites were regarded as the best evidence of the primitive segmentation, it was at first believed that the problem of the morphology of the Vertebrate head, as regards both number and nature of segments, had at last been solved by van Wijhe. His conclusion was that nine segments, four of which were pre-otic and five post-otic, enter into the formation of the Vertebrate head, or at least the Selachian head.

Yet one who studies the literature of the decade and a half that has elapsed since van Wijhe wrote his famous paper must conclude, from the great divergence of opinion which still prevails among the most competent investigators as regards both nature and number of head segments, that the problem is "noch nicht aus der Welt geschafft." According to Froriep, Kastschenko, and Rabl, the segments of the pre-otic and post-otic regions are of a fundamentally different kind. Furthermore, while Rabl ('92) finds not over three segments in the entire pre-otic region, Dohrn ('90) finds in the same region twelve to fifteen segments, serially homologous with trunk segments. These, indeed, represent extremes of opinion, for the majority of morphologists agree with Gegenbaur and van Wijhe that pre-otic segments are few but comparable with trunk segments. The chief causes of the present disagreement of morphologists are two. In the eager search for evidence of *segments* investigators have often failed (1) to control their results, based upon the study of a single organ system, by a comparison of the *actual* conditions which obtain in other organ systems in the same organism; and (2) to control conclusions based upon a single organism by appeal to the facts and conclusions of comparative anatomy and embryology. As the result of the healthful scepticism of such accurate observers as Froriep, Kastschenko, and Rabl, the necessity for such control now seems too obvious to need repetition here.

While morphologists (excepting Gegenbaur) in attempting to elucidate the problem of cephalic segmentation have based their conclusions chiefly on the study of the mesodermal segments, — since these have seemed to afford the best criteria of segmentation, — yet other embryonic structures have also been studied, viz. the segments of the central nervous system, or "neuromeres," the nerves, the epibranchial organs, the blood-vessels, and the visceral arches.

It is well known that in embryos of all classes of Vertebrates the central nervous system shows a segmentation which consists in a series of constrictions and dilatations extending throughout the length of the neural tube, giving to it a beaded appearance. In the trunk the nerves have a definite relation to the segments of the spinal cord, the "myelomeres," as I shall call them, adopting the term introduced by McClure ('89), and it is believed that the cranial nerves also have definite relations to the segments of the brain, the "encephalomeres," although their relations are less clear. Even if we believe with Ahlborn ('84*) and Froriep ('94) that the nervous system is segmented in adaptation to associated segmental structures, it is not *a priori* improbable that the number of primitive segments in the Vertebrate may be shown by the number of neural segments, for in some Invertebrate embryos segmental cephalic ganglia appear even when most other traces of mesodermal segments and related sense organs have (it is believed) disappeared.

In view of the present discrepancy between the results based upon the study of neuromerism and those based upon the study of mesomerism, it devolves upon one who attempts to elucidate the question of cephalic segmentation in Vertebrates by using the segments of the central nervous system as criteria, to show the comparability of encephalomeres with myelomeres, not only structurally, but also in relation to nervous outgrowths, and to those divisions of the mesoderm on which the segmentation of the motor nerves ultimately depends. The interdependence of motor nerve and muscle has seemed so evident that morphologists have not hesitated to make the number of cranial nerves conform with the number of somites previously determined by them. Yet the majority of investigators of the segments of the encephalon have failed to take into consideration the relation of these to the segments of the mesoderm, and consequently we find in the literature upon neuromerism a diversity of opinion such as we have learned to expect in results based upon insufficient knowledge.

SUMMARY OF RESULTS OF FORMER INVESTIGATIONS ON THE SEGMENTATION OF THE ENCEPHALON.

The results of former investigators concerning the number of encephalomeres and their nerve relations may be summarized in the form of two tables. Table I. shows the number of segments as determined by previous investigators, as well as their relation to the primary vesicles of the brain. The total number of segments has been given in the cases where it has been stated by the observer. The observations of

TABLE I.—ENCEPHALIC SEGMENTS.

			F.B.	M.B.	H.B.	Total
MAMMALS.	'42	Bischoff . . . Dog			6	
	'69	Duray . . . Ox		8?	6	
	'77	Mihalkovics . . Rabbit			5-6	
	'86	Kupffer . . . Sheep, Mouse, Man			5	
	'89	Prenant . . . Swine			5	
	'91	Zimmermann . . Rabbit	2	3	8	13
'92, '92'		Froriep . . . Mole	2	3	7	12
	'95	Broman . . . Man			7	
BIRDS.	'55	Remak . . . Chick			5-6	
	'77	Mihalkovics . . "			5-6	
	'85	Rabl . . . "			6-7	
	'87	Béraneck . . . "	2	1	6	9
	'89	Platt . . . "	1	1	6	8
	'90	McClure . . . "	2	2	6	10
'91		Zimmermann . . "	2	3	8	13
REPTILES.	'84	Béraneck . . . Lizard			5	
	'87	Orr . . . "	2	1	6	9
	'85, '89	Hoffmann . . . "			7	
	'85, '89	Hoffmann . . . Tropidonotus			7	
	'90	McClure . . . Lizard	2	2	6	10
	'91	Clarke . . . Alligator			5	
'92		Herrick . . . Snake			5-7	
AMPHIBIANS.	'75	Goette . . . Bombinator			?	
	'86, '93	Kupffer . . . Salamandra	5	3	?	
	'90	McClure . . . Amblystoma	2	2	5	9
	'91	Waters . . . "	3	2	5	10
	'92, '92'	Froriep . . . Salamandra				4
	'92, '92'	Froriep . . . Triton				5
'92		Wiedersheim . . Salamandrina	?	?	?	?
FISHES.	'75	Dohrn . . . Teleostei			8-9	
	'84, '85	Kupffer . . . "		8	5	
	'87	Scott . . . Petromyzon		8	5	
	'89	Platt . . . Salmon			5	
	'91	Waters . . . Cod	3	2	6	11
	'91	Zimmermann . . Acanthias	2	3	8	13
	'93	Kupffer . . . Acipenser	5	3	5	18
	'94	Kupffer . . . Ammocetes		8		
	'94	Locy . . . Squalus	8	2	6	11
	'96	Locy . . . "	3	2	6 (8)	14-15

investigators upon neuromerism have been seldom, if ever, so far extended as to determine the number of segments finally included in the head. The reason for this has been that the hindbrain neuromeres disappear before their relations to the posterior limit of the cranium can be determined. Table II. gives the nerve relations in different Vertebrates,

TABLE II. — ENCEPHALIC SEGMENTS AND NERVE RELATIONS.

		F. R. M. B. H. R.															
		1	2	3	1	2	1	2	3	4	5	6	7	8	9		
No. of Segmental Divisions.																	
'84	Béraneck																
'87	Béraneck	I	II														
'87	Orr	I	II														
'89	Hoffmann																
'89	McClure																
'89	McClure																
'89	McClure																
'89	Platt																
'89	Platt																
'89	Salmon																
'89	Chick																
'91	Waters																
'91	Waters																
'91	Amblystoma																
'91	Zimmermann																
'91	Zimmermann																
'91	Chick																
'91	Zimmermann																
'91	Herrick																
'92	Snake																
'92	Mole																
'95	Squalus	I	II														
'95	Loey																
'95	Broman																
'96	Man																

so far as they have been studied. In both tables it has been impossible to exclude much that is theoretical, and in view of this fact general conclusions are obviously dangerous. One important result, which should be borne in mind during the discussion of the evidence presented in this paper, is established, viz. the constancy, in all classes of Vertebrates, of five "hindbrain neuromeres" ("Falten" or "vrais replis"), and of their nerve relations. When *six* have been counted, usually the Anlage of the cerebellum has been included with them, and when *seven* (see Hoffmann, '90), another fold behind the true fifth neuromere has been counted. There is consensus of opinion that from the third "hindbrain neuromere" (designated in Table II. as 5, and as V in my figures) the acustico-facialis nerve takes its origin. In counting hindbrain neuromeres, then, this may safely be used as a check. In regard to the presence of true neuromeres, comparable with those of the hindbrain, in the region of the encephalon anterior to the hindbrain, much is theoretical, and, as I believe, uncritical. Morphologists have naturally been more or less prejudiced in favor of the view that a serially homologous segmentation extends throughout head and trunk. This preconception has led to the search for resemblances at the risk of disregarding differences which obviously exist, and as a result structures in the encephalon which are morphologically incomparable with the myelomeres have been homologized with them. Moreover, this has been done in utter disregard of their relations to the segments of the mesoderm.

The study of neural segments and their relations to nerves and somites in embryos of *Squalus acanthias* has given me some facts bearing on the problem of cephalic segmentation, which are, so far as I know, new. The conclusion which I have reached is as follows. *In S. acanthias there exists in early stages a continuous primitive segmentation of the nervous system serially homologous throughout head and trunk,—the "neuromeric" segmentation.* In later stages there appears in the encephalon a secondary (in time) segmentation resulting in the so called vesicles, which are not serially homologous with the segments of the myelon, but give rise to an anterior cephalic tract, which is a region *sui generis*.

In the following discussion I propose (1) to trace the development of neuromeres; (2) to compare the structure of the segments of the encephalon with those of the myelon; and (3) to note the relation of the neuromeres to the sensor and motor nerves, to the mesodermal somites, and to the visceral arches. I shall begin with the description of the first appearance of neural segmentation in the embryo.

I. Locy's "Neural Segments" or "Metameres."

a. MATERIAL.

Much of my material was collected with a view to the study of the "neural segments" or "metameres" described by Locy ('94 and '95). In a preliminary paper, which appeared with numerous illustrations in the "Anatomischer Anzeiger," 1894, Locy affirmed the discovery of "neural segments" in embryos of *Squalus acanthias*¹ at stages preceding the formation of the medullary folds and "before the mesoblast has, to any extent, become divided into somites." He therefore believed that these "epiblastic segments must be independent of any formative influence of the segments of the mesoblast." This discovery is interesting, and, if confirmed, one of most fundamental importance. I have therefore collected a large number of *Squalus* embryos in early stages of development, in order to confirm, if possible, Locy's results.

S. acanthias is abundant along the coast of Massachusetts in early summer, and the embryos are very easily obtained. My collecting was done at Rockport, Massachusetts, during the months of July and August, 1894, 1895, and 1896, and the number of specimens obtained exceeds twenty-five hundred. Locy has well insisted on the necessity of abundant material in closely connected stages of development.

The killing agents which I have used were (1) Davidoff's corrosive sublimate-acetic; (2) Kleinenberg's picro-sulphuric (undiluted); and (3) a mixture of Kleinenberg's picro-sulphuric (1 vol.), with $\frac{1}{2}\%$ chromic acid (3 vol.), especially recommended by Locy.

In this material were more than two hundred and fifty embryos corresponding to Balfour's stages C, D, and E. The specimen which shows Locy's "neural segments" best was killed in Kleinenberg's picro-sulphuric mixture (Plate 1, Figs. 1 and 2). I cannot recommend the mixture composed of picro-sulphuric and chromic acids, since specimens killed in it were not well preserved histologically. Davidoff's corrosive sublimate-acetic seems to me the best for general purposes of all the killing agents I have used, and consequently most of my material has been so killed. For the special study of the development of the nerves and the fibre courses in the wall of the brain, I have used material killed with vom Rath's fluid, followed by pyroligneous acid. This method I regard as most valuable, since with it nerve fibres are differentiated by

¹ *Squalus acanthias* (Linnaeus, 1748), synonymous with *Acanthias vulgaris* (Risso, 1826).

the precipitation of osmium in the very earliest stages of development, and it has given me results which I have been able to obtain in no other way. For staining sections Kleinenberg's hæmatoxylin has been used chiefly, while Heidenhain's iron hæmatoxylin and Grenacher's alcoholic borax carmine have both given excellent results.

b. METHOD OF STUDY.

In studying Locy's "neural segments" in *Squalus* embryos, reflected light was used, and in consequence low powers of the microscope were necessary. I have used constantly a small Zeiss stand in which the upper half of the stage and the superstructure revolve on the lower half of the stage, and his objective A and ocular I. My method of procedure has been, first, to make with the aid of a camera lucida an outline of the embryo cleared in clove oil and viewed as a transparent object. The irregularities of the edge of the neural plate may thus be represented accurately, and may serve as landmarks in the subsequent study of the specimen as an opaque object. After the outline drawing has been made, the specimen is transferred to a watch glass filled with alcohol. Now the important question is illumination. In order to bring out the delicate structures along the edges of the neural plate, oblique illumination should be used, since it brings into strong contrast the shadows and the high lights. The embryos should be rotated, so that light may be obtained successively from all directions and thus the chance of deception by false lights avoided. As the embryo is studied chiefly from the ventral side (for reasons given by Locy), careful manipulation with brush and needle is necessary in order to remove the yolk, which would otherwise obscure the edges of the neural folds. In studying these surface conditions, I have found a very faint hæmatoxylin stain and a black background to be of advantage.

In representing the specimen under observation, I have not had recourse to photography, but have made as faithful a representation as possible with pencil, seeking to preserve the relative values of light and shade. Since it is possible by careful illumination to increase the contrast of light and shade to a considerable amount, it is well to study the same embryo with different kinds of illumination. In this way it is possible to determine more satisfactorily what is permanent and what is not. The study of the segments is by no means easy, and the labor is considerable because it is necessary to study so many individuals. It is evident from a comparison of Locy's photographic representations, given in his final paper ('95), with his drawings, that the latter are,

probably for the sake of clearness, semi-diagrammatic in character. While his photographic reproductions show absolutely no segmentation in the early stages, his drawings on the contrary show in these same stages "segments" as clearly marked as those of later stages. Photography is obviously unsatisfactory as a means of reproducing these delicate structures.

Before taking up the consideration of the evidence which I have obtained from my studies, it is well to give a brief review of Locy's results. In his final paper ('95) he qualified his statement that the segmentation is solely epiblastic, since he discovered in sections that it may be found in both mesoderm and ectoderm. He therefore concludes that the segments seen in surface study are the remnants of a primitive metamorphism of the Vertebrate body. The more important points in Locy's description may be briefly summarized as follows. The evidence of segmentation appears first in the non-axial part of the embryo, i. e. along the thickened blastodermic rim. The segments later extend along the lateral margin of the neural plate from the anterior unsegmented tip of the embryo backward into the non-axial part. The segments are most clearly seen in "marginal bands along the neural plate," though "in the trunk region the lines of division may be traced inward toward the median furrow. This is probably due to the appearance of the mesodermic somites in that region." The "marginal bands," he thinks, "represent the dorsal nerve cord."¹ "These segments, once established in this very early stage, may be traced onward in an unbroken continuity until they become the neuromeres of other observers, and sustain definite relations to the spinal and cranial nerves." In the conclusion of his preliminary paper Locy writes, "No one is likely to question but what the segmented condition I have described represents a survival" (i. e. of an ancestral segmentation?). My own observations on embryos of *S. acanthias* lead me to question in large part the accuracy of Locy's observations, as well as his interpretations.

c. DESCRIPTION OF LOCY'S "NEURAL SEGMENTS."

I shall now give an account of the conditions, as I have found them, in the head region of a shark embryo with 6 to 6½ somites.² This

¹ In his final paper Locy speaks of the "neural folds or ridges" as "divided throughout their length into a series of segments."

² I count the somites beginning with van Wijhe's 7th somite (somite 7 of my figures), the myotome of which becomes the first segment of the lateral trunk musculature (van Wijhe).

stage has been selected to begin with, because it gives the strongest evidence that I have seen of a segmented condition in the neural plate. I shall describe first two embryos which represent fairly well the conditions I have found at this stage. These two embryos are represented in Figures 1, 2, and 3, Plate 1. The neural or "medullary" plate is seen to be a spatula-like expansion of the anterior end of the embryo, raised somewhat above the blastodermic area. Figure 1 (Plate 1) represents an embryo viewed from the dorsal side; the neural plate, it will be observed, is not perfectly flat, for its edges bend slightly ventrad and a shallow depression extends along its median portion. The chorda, lying in the axis just beneath the neural plate, causes a slight elevation of the floor of the groove in the median line. Anteriorly the chorda passes into the common tissue which later becomes differentiated into entoderm, mesoderm, and chorda. The anterior more expanded portion of the neural plate has been called the "cephalic plate." At the posterior portion of this cephalic plate its lateral wing-like expansions undergo their greatest bending ventrad. The posterior or trunk portion of the neural plate extends back into the tail folds and along the embryonic rim. I do not wish to seem to imply by this statement that the tail folds and the embryonic rim become included in the neural tube, because, although in general I believe in the concrescence theory, I do not find in the *continuity* stated above any evidence of addition to the posterior part of the neural plate by a concrescence of the tail folds and the embryonic rim.

In the dorsal view of the embryo shown in Figure 1, Plate 1, little or no evidence is afforded in either cephalic or trunk regions in support of Locy's contention that the edges of the neural plate are segmented. We see only that the edges of the plate are slightly and *irregularly* lobed, and not in the true sense segmented. *For the lobes on the opposite margins of the plate do not correspond in number or position, neither do they show any definite relation to the mesodermal somites, as seen in the cleared specimen.*

Figure 2, Plate 1, shows the same embryo viewed from the ventral side, and gives the strongest evidence I have seen of Locy's interpretation of the condition of the neural plate. The "segments" appear much more marked in embryos of this stage when viewed from the ventral side, for reasons already stated by Locy, who has well insisted upon the importance of ventral views. There are several reasons, however, for regarding the structures which appear along the edges of the neural plate as not true segments. These so called segments, even in the cephalic

region, are not equally distinct, it being very difficult, if not impossible, to determine the boundaries of some of them. They also differ considerably in length and apparently without any regularity, a condition not easily reconciled with the interpretation of them as true segments. It would certainly be impossible even in this specimen to point out with certainty corresponding segments on opposite sides of the cephalic plate. In the trunk region of the same specimen no correspondence between somites and "neural segments" is seen. However, a faint lobing of the inner margin of the tail fold is seen on the right side of the embryo. Locy's ('95, p. 519, Fig. 29) description of a stage as close to this as any figured by him is as follows: "They [the segments] appear like a row of beads running along the ventrally recurved margin, and extend with great distinctness the entire length of the embryo. Those in the trunk region are continuous with those of the head, and pass into the latter without any transition forms. There is, however, some individual variation in size of the neuromeres, and they are not absolutely symmetrical on the right and left sides, but the significant thing is, [that] there is uniformly the same number on each side in a given region, such as the hindbrain, or the brain region as a whole. . . . There seems now to be a natural landmark separating the 'cephalic plate' from the rest of the embryo; this is an abrupt downward bending in the medullary folds, which, as I have determined, lies just in front of the future origin of the vagus nerve. There are eleven *metameres*¹ in the lateral margins of the cephalic plate, including the ones embraced in this fold." The accuracy of this conclusion I shall discuss in treating of the question of the limit of the cephalic plate (p. 162). I wish here only to call attention to the fact that none of the reproductions of Locy's photographs, with two possible exceptions (his Figs. 2 and 23), show a segmentation of the neural folds in either the trunk or the embryonic rim.

If now we turn to Figure 3 (Plate 1), we find an embryo of about the same stage as that shown in Figures 1 and 2; at least, it has the same number of somites (6 to 6½). The conditions are these. The "segments" at the margin of the neural plate differ markedly in distinctness, and are irregular in size. In the region of the cephalic plate — the posterior boundary of which is marked by the arrow — the number of segments on the right and left sides is not the same. I was not able to assert this with so much confidence in regard to the embryo of Figures 1 and 2, since in that embryo the limits of the cephalic plate were less clearly defined. If the segments of the two sides of the neu-

¹ *Italica mine.*

ral plate in Figure 2 do not admit of a satisfactory comparison, neither is it possible, even with a prejudice in favor of finding uniform conditions, to state exactly which segments of Figure 3 correspond to those of Figure 2.

An examination of many embryos (more than fifty) in this stage of development—at which, in agreement with Locy, I have found that the segments are more clearly marked than at any other stage—has served only to establish the opinion that there is no constancy in their number in different individuals, nor agreement in number or position upon the two sides of the plate of a single individual. After an examination of a large number of embryos at this and closely related stages, I have been compelled to abandon my first opinion, which was based chiefly on the study of the embryos of Figures 1 and 2, and was favorable to Locy's contention. In no case that I have seen do the segments appear symmetrical, and in no case have I been able to determine a definite relation with the somites.

d. CONTINUITY OF THE "SEGMENTS."

My observations have of course not been confined to this most favorable stage. While the evidence given above, based on the study of embryos at a stage when the segments are most plainly seen, appears to my mind satisfactory proof that true segments do not exist at this time, the study of embryos in both earlier and later stages shows that even these segments are only transitory structures. This evidence, though in a sense negative, is not without weight in the treatment of the question. It constitutes, it is true, neither proof nor disproof of the genuineness of the segments. It is, however, what we should expect, if we find the segments unlike in number and size on the two sides of the same embryo and in different embryos of the same stage. A want of continuity in successive stages is not, however, what we should expect if we were dealing with true segments. These structures would certainly have much less morphological value than is assigned to them by Locy, were they simply transitory and without definite relation to organs which appear in later stages. Locy believes that he has traced them "up to the time when they form neuromeres," but he by no means makes it clear how structures which appear "like beads" along the edges of the neural plate become transformed into *ventral* structures such as, according to his own account, the "neuromeres" are. "In the trunk region," he says ('95, p. 516), "the lines of division may be traced inwards toward the median furrow. This is probably due to the appearance of

the mesodermic somites in that region." In the head region, where somites do not similarly press upon the neural plate, it still remains for Locy to show how structures morphologically dorsal, as his "neural segments" are, become converted into structures morphologically ventral as well as dorsal, as are the "hindbrain neuromeres," for example.

My own evidence of their continuity in time is, as I have said, negative. Figure 4, Plate 2, represents an early stage with three or four somites. One sees the "marginal bands" of which Locy has spoken, but only the faintest traces of segments are visible. On one side—the right—they are exceedingly irregular. At this stage the lateral edges of the neural plate are not flexed ventrally, and such segments as are to be seen at all show best from the dorsal side. A quite regular segmentation is seen on the left side of the cephalic plate, yet the segments are by no means all of the same size or distinctness, nor do they equal in size the mesodermal segments. In the trunk region the lobes of the edge of the neural plate show no definite relation to the mesodermal somites, the boundary between two somites coinciding in some cases with the depression between lobes, in others with the apices or with other parts of the lobes. I wish to call especial attention to the fact that here, as in the embryos shown on Plate 1, *the segments are confined to the marginal bands*, and therefore do not extend into the median plate. Here, again, there is a considerable discrepancy between Locy's observations and my own.

I have found it impossible to trace definite segments into the later stages, for in these stages, before the closure of the neural tube, in the majority of specimens little or no evidence of segments along the cephalic plate can be seen.

Two embryos in later stages of development are seen in Figures 5 and 6, Plate 2. There is practically no evidence of segmentation or lobing of the edge of the medullary folds. The segments which Locy has numbered 1, 2, and 3 are visible in many specimens, in some very distinctly, as shown in his photographs; but behind them there is an irregularly sinuous or entirely smooth edge, as shown in my Figures 5 and 6, and in Locy's photographic reproductions. These three anterior segments, according to Locy, shift their position. Since, however, I do not find them constant in appearance and position, I have not been able to regard them as of morphological importance. It is worthy of note that they appear in the region of the neuropore, and that possibly they may be partly accounted for as the result of the difficulty of fusion

of the neural folds at this point (the angulus terminalis). Their late appearance is possibly also to be correlated with the late appearance of the anterior portion of the neural crest.

The evidence which I have given leads me to conclude that the so called neural segments cannot be traced into the "neuromeres" of later stages. Of the accuracy with which Locy has traced them I shall have more to say, when I speak of the limits of the cephalic plate.

c. INTERPRETATION OF THE EVIDENCE.

Locy interprets the "neural segments," as has already been stated, as "survivals of a primitively segmented condition of the body." In search for evidence to support this phylogenetic interpretation, he has studied the early stages of the Torpedo, Amphibians, and the chick.

Torpedo embryos (p. 531) are found to be "not so favorable for the study of the segments as Acanthias," yet "the number [of folds] in a given region in Torpedo corresponds to that in Acanthias." In the three Amphibian forms which Locy has studied (Amblystoma, Diemyctylus, and Rana) "there are *about* ten pairs of segments in the broadly expanded neural folds of the head." In the chick, "there are eleven segments in front of the first formed protovertebræ." Locy has also found (p. 539) that in the chick "*the walls of the primitive groove are also divided into segments that are similar to those that appear in the neural folds.*"¹

Owing to the evidence stated above, I am unable to regard the segments in *S. acanthias* as of phylogenetic value. Are they then artifacts, as suggested by Eycleshymer?² I do not think so. Several of the best fixing agents have been used by Locy and myself, and he has in addition observed these structures in living embryos. It is known, however, that different fixing agents cause differences in internal and external conditions, as the result of swelling or contraction. They may have served to intensify the distinctness of Locy's segments, yet it is hardly probable that they are the sole cause of them.

I believe that the segments are the results of unequal growth along the margin of the neural plate. It is obviously not necessary to

¹ Italics my own.

² Eycleshymer's ('95, p. 394) observations on Amblystoma do not agree with those of Locy. Eycleshymer states that "certain markings which might be interpreted as neuromeres are often observed in the neural folds, yet their arrangement is decidedly irregular, and one is led to believe that they indicate nothing more than artifacts caused by the killing agents." I have carefully examined Amblystoma embryos, at a stage when the neural folds are widely open, and my observations agree with those of Eycleshymer.

regard such irregularities of the edge of a rapidly expanding plate of tissue as of morphological importance. It is very significant that the segments show most prominently in the cephalic-plate region just before the edges of the plate begin to rise dorsally, for it is likewise at this stage that I find the first evidence of the disassociation of cells along the edges of the neural crest. Such a disassociation of cells, or even a rapid proliferation of cells, — which certainly does occur in this region, — would lead to such phenomena as those reproduced in Figures 1 and 2, Plate 1. An examination of cross sections of the cephalic plate (Plate 7, Figs. 55 and 56) before the edges have fused dorsally to form a closed tube shows that the neural crest is already differentiated from the tissue which will form the walls of the neural tube; it is differentiated as a region of rapid cell proliferation and of less compactly arranged nuclei. If the centres of cell proliferation were fixed, then we should have a segmented neural ridge, as affirmed by Beard ('88).

My interpretation differs from Locy's, since he finds the "neural ridges" segmented regularly, and considers the segments as survivals of an ancestral segmentation; whereas I find the edges of the neural plate irregularly and somewhat transitorily segmented, the irregularity and inconstancy of the segments precluding, in my opinion, a phylogenetic interpretation. Locy's results from surface studies seem to me to be a confirmation of those reached by Beard ('88), who, in studying the development of the peripheral nervous system in *Selachii*, found from the examination of sections that the neural crest is differentiated before somites appear, and that it is from the beginning segmented. Beard's conclusions have, however, never been confirmed, and have indeed been regarded by Dohrn ('90, p. 55) as quite untenable.

To demonstrate that Locy has not accurately traced the "neural segments" onward in unbroken continuity until they become the "neuromeres of other observers," I propose to discuss the relation of the neuromeres to the posterior limit of the cephalic plate.

f. LIMIT OF "CEPHALIC PLATE."

Locy ('95, p. 543) has stated that in early stages of the embryo, before the neural plate has formed a closed tube, head and trunk may be distinguished. "It is possible," he says, "in very young stages to draw a line indicating where the expanded part of the cephalic plate joins the non-expanded part of the embryo. . . . This is, in *Squalus acanthias*, just in front of the point where, subsequently, the vagus nerve begins. . . . In this animal, we may identify that part of the head which lies in front of

the vagus nerve by counting the first eleven neural segments. It will be merely a question of agreeing upon the number of primitive segments belonging to the vagus, to enable us to locate with definiteness the hindermost limit of the head. Besides being of use in other ways, this would enable us to say, even in the earliest stages, what is head mesoblast and what is trunk mesoblast."¹

I cannot see that Locy's determination of the limits of the cephalic plate helps us at all in the determination of the boundary of head and trunk. This boundary, as he states, has still to be determined. To fix the limits of head-mesoderm by a direct study of the mesoderm itself is quite as easy as to determine its boundary by the still hypothetical posterior boundary of the vagus region. According to Locy, the posterior limit of the cephalic plate separates neither what is pre-otic from what is post-otic, nor head from trunk.

My own observations on this point differ fundamentally from those of Locy, since according to my determination the line which separates the expanded cephalic plate from the region posterior to it marks the posterior boundary of the auditory invagination. This is of value, in so far as it enables us to distinguish those two regions — which on other grounds have always been held to be distinct — in stages earlier than was formerly possible. The posterior boundary of the cephalic plate is a clearly marked point at a stage before the neural folds begin to be raised dorsally, and it is situated just behind the region of greatest ventral flexure of the cephalic plate (marked by an arrow in Fig. 3, Plate 1). This point may be traced into later stages, until the neural plate is transformed into a closed tube, when it is seen that it corresponds exactly with the hinder boundary of the hindbrain neuromere numbered VI in my figures (Locy's 10th "neural segment"); opposite this neuromere, as has been stated by many observers, lies in early stages the centre of the auditory invagination. The thickened auditory epithelium extends anterior and posterior to this neuromere; but it is opposite this neuromere that the first invagination to form an enclosed capsule takes place (see Plate 3, Figs. 15 and 16). In later stages the ear capsule shifts backward, so that its centre comes to lie opposite the hindbrain neuromere numbered VII in my figures, which, as may be inferred from the statement above, lies in — or rather is afterwards differentiated from — the region behind the cephalic plate. I have been able to determine with certainty that the posterior limit of the cephalic plate

¹ Locy finds that in later stages segments are added to the occipital region from the region of the trunk (see Tables I. and II.).

is a fixed one from a stage with seven somites, until the plate no longer exists as such. That it corresponds with the posterior boundary of neuromere VI of my figures, I am able to state with equal positiveness. Not having found, as Locy has done, eleven segments in the cephalic plate, by counting which one could determine the limits of the plate, I have been obliged to resort to other means. My method of determination has been as follows. As a fixed point in all the stages examined, I have taken the mesodermal somite marked 7 in Plates 1 to 4. This, as I determine, is the most anterior somite which becomes innervated by a ventral spinal root; it therefore corresponds, I believe, with van Wijhe's 7th somite.¹ Anterior to this is formed a somite (van Wijhe's 6th), which in early stages possesses embryonic muscle fibres, but never becomes innervated by a motor root. Rabl ('92) said he could affirm with confidence that the somite (Urwirbel) which van Wijhe holds for the 6th or 7th head segment in an embryo with 48 somites is identical with that which he counts as the first trunk segment in an embryo of 76 somites. This mistake [?] of van Wijhe's, the accuracy of whose work in general is so well known, has led me to take especial pains to verify the identity of somite 7 in the stages most carefully examined, viz. from the stage with 6 to 7 somites, until after the neural tube is closed. Its identity has been determined as follows. I have carefully measured the distance from the constriction between van Wijhe's 2d and 3d somites—the mesodermic constriction which appears above the hyomandibular cleft—to the *partial* constriction anterior to van Wijhe's 6th somite. This distance measured in over two hundred embryos by means of camera-projection images, I have found to be practically constant, since it increases only very slightly as the embryo increases in length. Having thus determined the identity of this somite in successive stages, I have had a safe starting point for the determination of the posterior limit of the cephalic plate. I have measured the distance from the posterior cleft of van Wijhe's 7th somite, in the manner described above, to the posterior boundary of the widely expanded cephalic plate, and I have found this distance also to be constant. I chose to measure from the posterior boundary of van Wijhe's 7th somite, because by the measurement of this rather than a less distance the chances of error were diminished. The reader can verify the constancy of this distance by measuring the Figures (3 to 10) on Plates 1, 2, and 3, which were drawn with the aid of a camera, and are magnified forty-three diameters. *This distance is almost precisely the same as the distance from*

¹ Van Wijhe's 1^o occipital Somit. Rabl's 3^o distale Urwirbel.

the posterior boundary of somite 7 to the posterior boundary of neuromere VI, after the closure of the neural tube (see Figs. 7 and 10, Plate 3, and Fig. 6, Plate 2), and, as previously stated, the posterior boundary of the auditory invagination at first coincides with the posterior boundary of encephalomere VI. Again, and in direct confirmation of the evidence stated above, the posterior boundary of encephalomere VI is the posterior boundary of a greatly enlarged portion of the neural tube (Figs. 7-10, Plate 3), as one would naturally expect, if it coincides with the posterior boundary of the previously widely expanded cephalic plate. With this fact in mind it is interesting to compare the conditions I have found with Locy's results. I believe he would not contest the assertion that my encephalomere VI is identical with his neuromere 10 (Zimmermann's encephalomere 11), because its relation to the ear vesicle at the time this is formed makes its identification a simple matter. Locy ('95, p. 522) says of the auditory vesicle: "When first established its centre occupies the space of the segment marked 10. Sometimes, in its earliest stages, the circular area spreads over the space of the three segments marked 9, 10, and 11, but I should say from my observations that, more frequently, it is not so widely expanded. It always settles down in *Squalus acanthias* to occupy the position first indicated, and subsequently it is shifted backwards." This accords with my identification of his segment 10 with my encephalomere VI, and this conclusion is corroborated by his statement that "the segment marked 8 is seated above a depressed region in which the first visceral cleft appears," for that is precisely the position of the encephalomere IV of my figures. On page 528, however, he says, "When the ear vesicle first arises it makes its appearance opposite the *ninth* neuromere" (!). Again, in his Figures 6 and 9, Plate XXIX., "neural segments," which are described (p. 528) as 8 and 9, but which I believe to be segments 9 and 10 (as a comparison with my Fig. 46, Plate 7, shows), are numbered 7 and 8 (!). Here, then, are three conflicts. Despite the elusive nature of Locy's "neural segments," I am disposed to regard his neural segment 10 (opposite which, as he has twice stated, the auditory invagination occurs) as identical in position with encephalomere VI of my figures. If this be true, there is no room on the cephalic plate for his neural segment marked 11, since, according to my determination, encephalomere VII is differentiated from the region of the neural tube which lies *behind* the broad cephalic plate, and does not become clearly marked off from the spinal cord region before a considerably later stage (stage H of Balfour). Therefore, if Locy's neural segment 11 is identical in position with my en-

cephalomere VII, I see no escape from the conclusion that he has not "traced neural segments accurately up to the time they form neuromeres." It is hardly conceivable that he will bring forward in this instance the explanation previously offered in a similar case of mistaken identity, that somehow, between the stage with an open neural plate and a closed tube, segment 10 (neuromere VI) has *insidiously* come to assume the position previously occupied by his segment 11, and that segment 11 has been crowded backward. And it is likewise improbable that he would follow this explanation with another, — as he did in the case mentioned, — that encephalomere VI of my figures represents the "combined vesicle" of his segments marked 10 and 11.¹

I now turn to the study of what I regard as the true primitive segmentation of the nervous system, — the so called neuromeric segmentation.

II. The "Hindbrain Neuromeres" in *S. acanthias*.

a. DEFINITION OF THE TERM "NEUROMERE."

In the preceding description the term "neural segment," or simply "segment," has been used as a non-committal term for structures of such different morphological value as those described by Locy under that name and the regular foldings of the neural tube. Locy ('95) has used the term "metamere" as synonymous apparently with his term "neural segment." Since, however, the term "metamere" is applicable by usage only to the successive similar parts of the body as a whole, it cannot be applied wisely to the successive parts of a single organ system, such as the nervous system.

Ahlborn ('84*) was the first to use the term "neuromere," and he applied it to all the successive similar segments of the central nervous system. Béranek ('84) applied the term "replis medullaires" and Kupffer ('86) the term "Medullarfalten" to the regular foldings seen in the brain region of Vertebrate embryos, those of the hindbrain being given by Béranek the special appellation of "vrais replis." Since the

¹ In a paper which comes to hand just as this goes to press, Locy ('97) states that he finds two sets of vesicles in the brain of chick embryos. Of these the first set, numbering seven in all, called by Locy "optic vesicles," are very ephemeral in existence, and have nothing whatsoever to do with the second set, called by him "brain vesicles." In *Acanthias* (*Squalus*) also he finds at least nine pairs of "optic vesicles," likewise very transitory. The exact relation of these to the "metameres" or "neuromeres" he does not state.

English equivalent of Kupffer's "Medullarfalten" and of Béraneck's "replis medullaires" (medullary folds) is used with an entirely different meaning from that intended by these writers, Orr ('87, p. 335) employed the term "neuromere" for the folds due to symmetrical constrictions seen in the hindbrain and the thalamencephalon, and distinctly stated that in Lizard embryos no neuromeres are found behind the vagus nerve. This limitation of Ahlborn's term has not, however, been accepted by later investigators. McClure ('89 and '90) again extended the term neuromere so as to include all the constrictions and dilatations of the neural tube, and classified neuromeres into: (1) *myelomeres*, due to constrictions of the myelon; (2) *encephalomeres*, resulting from constrictions of the encephalon. The latter term had, however, been previously used by Wilder ('89) for the large encephalic vesicles. Zimmermann ('91) adopted the term encephalomere, although he did not attempt to compare "Encephalomeren" with "Myelomeren," and Froriep ('94) used the term for theoretically homodynamous segments of the neural tube in the region of the head. He stated that the encephalomeres may correspond with neuromeres, but that this correspondence is not self-evident.

I shall adopt the nomenclature proposed by McClure ('89 and '90). In my account of the segmentation of the brain I shall begin with the conspicuous constrictions and enlargements of the hindbrain, which have uniformly been regarded by morphologists as typical neuromeres or encephalomeres. Orr's ('87) criteria for neuromeres, based on the study of the hindbrain of Lizard embryos, are as follows: (1) "Each neuromere is separated from its neighbors by an external dorso-ventral constriction, and opposite this an internal sharp dorso-ventral ridge, so that each neuromere (i. e. one lateral half of each) appears as a small arc of a circle." (2) "The constrictions are exactly opposite on each side of the brain." (3) "The elongated cells are placed radially to the inner curved surface of the neuromere." (4) "The nuclei are generally nearer the outer surface, and approach the inner surface only toward the apex of the ridge." (5) "On the line between the apex of the internal ridge and the pit of the external depression, the cells of adjoining neuromeres are crowded together, though the cells of one neuromere do not extend into another neuromere." Later investigations have served only to confirm this clear analysis of the structure of a neuromere.

b. DEVELOPMENT OF HINDBRAIN NEUROMERES.

Previous investigators have assumed that the hindbrain neuromeres possess the same characteristics at their first appearance that they do in

later stages, whereas it will be shown in *Squalus* that this is not the case.

The want of abundant material of early stages felt by investigators in most cases is not a hindrance in the case of *Squalus*, for the early stages are as easily obtained as the later ones. In the study of the development of neuromeres, I have made use, first, of specimens very lightly stained in hæmatoxylin and mounted *in toto* in balsam, and secondly of the usual cross, frontal, and sagittal sections. The series of embryos represented in Plate 3 is chiefly of value in showing the neuromeres in successive stages, and the relations of the masses of cells composing the neural crest, or ganglionic Anlagen (colored blue in the figures), as seen in cleared specimens. The neural tube is represented as seen in optical section, while the other structures of the right half of the embryo are projected upon the median plane.

The earliest evidence of hindbrain neuromeres which I have found is seen in embryos of 14 or 15 somites in which the cephalic plate has not closed in the hindbrain region. In most embryos with that number of somites the plate is already closed, but in cases where it has not, neuromeres IV, V, and VI are seen as thickenings of the lateral walls of the hindbrain before its closure. Usually closure takes place, as in the chick, first in the region of the so called trigeminus Anlage, and later in the region of neuromere V, the most anterior portion of the cephalic plate remaining open as the neuropore until considerably later stages. Figure 7, Plate 3, shows that in embryos of 14 to 16 somites (in the specimen figured, after the closure of the cephalic plate) four expansions of the neural tube in the hindbrain region are differentiated (neuromeres III, IV, V, VI). The hinder boundary of neuromere VI marks the former posterior boundary of the cephalic plate. The figures show (and this is a point of considerable importance in considering the morphological value of neuromeres) that each neuromere corresponds to the region of a dorsal as well as a ventral expansion of the neural tube, and that the neuromeres are separated from one another by both dorsal and ventral constrictions, which are to be seen both in sagittal sections and in cleared specimens.

Frontal sections at this stage give additional evidence concerning the structure of hindbrain neuromeres. A frontal section just below the axis of the neural tube is shown in Figure 22, Plate 5. The section shows that the cephalic plate is still open in the region of the forebrain. The dorsal portion of the mesoderm in the region of van Wijhe's 2d and 3d head somites (2 and 3) is cut on the right side only, the sections not

being exactly frontal on account of the torsion of the embryo. The lateral walls of the neural tube are seen in the figure to be thickened in that region which lies just posterior to the constriction opposite van Wijhe's 3d somite. A comparison of many frontal and sagittal sections leaves no doubt that this thickening lies in the region of neuromere IV. That expansion of the neural tube which lies between the 2d and 3d somites, and which is separated by an external constriction from neuromere IV behind and from the midbrain vesicle (encephalomere II of my figures) in front, is the most anterior of the primary expansions or encephalomeses of the hindbrain. It has been called by Zimmermann ('91) "Hinterhirn." This corresponds to the third expansion of the neural tube in the chick (Fig. 44, Plate 7), as may be determined by its relation to the acustico-facialis Anlage and the auditory invagination. Failure correctly to identify this vesicle in the chick led Miss Platt ('89) to call the second vesicle, viz. the primary *midbrain*, the *hindbrain*.

At a later stage, when 17 to 18 somites are differentiated, a well marked local thickening in the posterior half of encephalomere III appears.¹ A frontal section of an embryo at this stage, showing neuromere IV as a local thickening posterior to neuromere III, is seen in Figure 23, Plate 5. Encephalomere III is separated by a constriction from encephalomere II. At this stage, then, only four of the hindbrain neuromeres (III, IV, V, and VI) are differentiated, and the conditions remain the same when one more somite is formed.

In a similar frontal section of an embryo with 19 somites, such as is represented in Figure 24, four symmetrical thickenings of the lateral walls of the hindbrain (III-VI) appear. Opposite neuromere V lie the cells of the Anlage of the acustico-facialis nerve (blue), and opposite neuromere VI the thickened auditory epithelium. Neuromere VII is not present at this stage, and it does not begin to be differentiated until after one or two more mesodermal somites are formed, when a faintly marked dorsal and ventral dilatation appears in the region of the neural tube just behind neuromere VI (Fig. 9, Plate 3). The lateral walls of this neuromere never become so markedly thickened as the walls of the other neuromeres, nor does the neuromere show a constriction at its posterior border before the embryo reaches the condition of Balfour's stage H, and then only a faintly discernible one. A cross section

¹ Such a secondary subdivision of encephalomere III. ("Hinterhirn") occurs in the chick as in *S. acanthias*. I regard the primary vesicle as of different morphological value from that of its subdivisions, for reasons which will be made more apparent when the relations of the vesicles are studied.

through neuromere IV, which serves to show how greatly thickened the lateral wall is at this stage, is shown in Figure 32, Plate 5. The dorsal wall of this neuromere is considerably thicker than that of the neuromeres anterior and posterior to it, possibly because few cells are proliferated from this neuromere to form the ganglionic Anlage or neural crest.

I pass now to a description of the hindbrain neuromeres (encephalomes) at a stage with 28 or 30 somites (Balfour's stage H). Since at this stage the neuromeres are clearly differentiated, and the thinning and expansion of the roof of the hindbrain have progressed very little, this is a most favorable stage for the study of the structural and histological peculiarities of the hindbrain neuromeres.¹ Figure 13, Plate 3, represents a cleared specimen at this stage, and Figure 25, Plate 5, a frontal section of the same. Opposite neuromere III (Fig. 25) lies part of the trigeminus Anlage; opposite neuromere V lie the cells of the acustico-facialis Anlage; and opposite neuromere VI lies the thickened auditory epithelium, which is just beginning to invaginate. The acustico-facialis Anlage always remains in relation with neuromere V, so that this serves as an excellent starting point in counting the neuromeres. In order to get a clear conception of the structure of the neuromeres, cross, frontal, and sagittal sections are necessary. The series represented in Figures 36-38, Plate 6, are frontal sections taken at different levels (α , β , γ , Fig. 40, Plate 6) in the medullary tube. Only the right wall of the medullary tube in the region of neuromeres IV and V is shown in detail. The first section (Fig. 36) is dorsal, in the region of the "Deckplatte." In this section it is seen that what Orr ('87) has said for the Lizard (see page 167) is true for *Squalus*. The section reproduced in Figure 37, more ventral than Figure 36, shows that the conditions which obtain in the region of the lateral zones are somewhat different from those of the dorsal zone. Since no sharp internal ridge exists, each lateral half of a neuromere does not appear in section as an arc of a circle, but as a thickening of the wall of the medullary tube. The cells and nuclei are fewer in number and more crowded in the region of constriction between neuromeres. Although there is no inner concavity at this level, the cells and nuclei (Fig. 37) show a radial arrangement similar to that shown in Figure 36. The ventral section (Fig. 38) differs in no essential respect from the dorsal one. I have chosen these two neuromeres (IV and V) for description, since they with neuromere VI

¹ The head somites, likewise, appear at this stage most clearly differentiated. It is, in fact, the "acranial stage" of the embryo.

show the characteristics stated above in the most marked way. Only a faint external constriction, without internal constriction or ridge, separates neuromere VII from the region of the spinal cord.

At a stage with fifty somites (Balfour's stage K) the structure of the neuromeres is slightly but not materially changed. In Figure 17, Plate 3, is represented an embryo of this stage, viewed as a transparent object. Figures 26-29, Plate 5, show four frontal sections of such an embryo, Figure 26 being the most dorsal, and Figure 29 the most ventral of the series. Figure 26 shows that the most dorsal portion of the Deckplatte has become very thin, being only one layer of cells thick. The constrictions and dilatations are only faintly shown, the nuclear arrangement being the same in the region of the constriction as in the region of dilatation. Figure 27, more ventral than Figure 26, though still in the region of the Deckplatte, shows the conditions, both nuclear and cellular, to be almost precisely the same as in Figure 36, Plate 6. The internal ridges, or cusps, are sharp, and the cells in the region between the internal ridge and external constriction are closely crowded together. It is to be noted that the separation of the lateral walls of the hindbrain is least marked in the region of neuromere VI, opposite which the ear capsule lies (compare Fig. 17, Plate 3). Figure 28 seems to show that the neural walls have become considerably thickened in the region of the lateral zones. There is no doubt that the lateral zones are absolutely and relatively thicker than at the stage last described, while the neuromeres have increased in length. It is to be observed that this thickening is accompanied by a change in the outline of the lumen of the tube, vertical grooves appearing in the place of the vertical ridges of the more dorsal sections. In the most ventral of the sections, Figure 29, the internal ridges appear again, though the concavity of the inner surface of each neuromere in the antero-posterior direction is only faintly indicated.

During stage K, as the result of the great expansion and thinning of the Deckplatte in the region of the medulla oblongata, the neuromeres come to affect only the lateral zones. Locy ('95, pp. 524 and 525) notes changes in the appearance of the "neural segments" at this stage, the explanation of which he does not state with precision. His opinion seems to be, however, that a union of part of each of the original segments with the segment lying just in front of it, accounts for this condition. An examination of the series of Figures 7 to 21 of my Plates 3 and 4, and of the frontal sections of Plate 5, shows that no such fusion of neuromeres takes place. The constrictions and ridges between

neuromeres never shift their position, the only change being a gradual assumption, by each of the local thickenings, of an inner concavity in the region of the lateral zones.

Frontal sections of an embryo 15 mm. long show that dorsally all traces of the neuromeres are lost. A frontal section in the region of the lateral zones from an embryo of this stage is represented in Figure 30, Plate 5. A great separation of the lateral walls of the medulla is seen to have taken place in the region of neuromeres III, IV, and V. At this stage only do the neuromeres possess the characteristics described by Orr for the Lizard (see page 167). While the external constrictions are only faintly shown, owing to the increase of the "white substance" on the sides of the medulla, the internal ridges and concavities are well marked. From this stage onward the neuromeres begin to disappear. In embryos of 40 mm. to 50 mm., neuromere VI, in relation with the facialis nerve, is the most clearly marked of the neuromeres.

Before passing to an examination of the evidence of neuromeres in the trunk region, I wish to emphasize the fact that the hindbrain neuromeres cannot be regarded as structures dependent upon the pressure of mesodermal somites. Being local thickenings of the lateral wall of the neural tube they are obviously inexplicable on such a simple mechanical basis. They are structural differentiations of the tube in regions where the mesoderm has not yet extended, — that is, in the dorsal and lateral portions of the tube, the mesoderm of the head being still ventral in relation to the neural tube.

c. SUMMARY.

In the preceding study of the hindbrain neuromeres in *S. acanthias*, I have supplemented Orr's criteria (applicable to later stages) by a description of the structure of the neuromeres in *Squalus* in earlier stages of development, i. e. in embryos of 14–50 somites. The characteristics possessed by hindbrain neuromeres in these earlier stages may be summarized as follows. Each neuromere is separated from its neighbor by an external constriction, which passes entirely around the neural tube. There is dorsally and ventrally an internal ridge corresponding to this external constriction; but the ridge vanishes in the region of the lateral zones, being replaced by an internal depression or groove. The nuclei of the lateral wall are, however, still arranged (Fig. 37) in a manner which approximates that of the region of the internal ridges, notwithstanding that the thickening of the lateral wall of the neuromere has

actually obliterated all surface evidence of such a condition. Each hind-brain neuromere, therefore, consists of a lateral thickening and a dorsal and ventral dilatation of the wall of the neural tube. The constrictions are exactly opposite on the two sides of the brain. The elongated cells are placed radially to an imaginary point situated in the middle of the thickening of the wall opposite. The nuclei are generally nearer the outer than the inner surface, and approach the latter only in the region of the constriction between the neuromeres. In this region the cells are more crowded, but the cells of one neuromere do not extend into the adjacent neuromeres.

The hindbrain neuromeres, being structural differentiations of the walls of the neural tube, are not to be explained as the result of a simple mechanical process. The essential similarity of these serial groupings of nerve cells to the metameric ganglia of Annelids will, I believe, impress others as well as myself. A reconstruction of the neuromeres as they appear in this typical condition is shown in Figure 40, Plate 6.

III. The Neuromeres in the Trunk Region.

a. DEVELOPMENT OF MYELOMERES.

It might seem that a more natural sequence in the study of neuromeres than the one here followed would be to pass from the simpler conditions which obtain in the trunk to the more complicated ones in the head region. Instead of this, I follow the historical sequence, having begun with the "Kräuselungen," or foldings, first seen by observers in the region of the hindbrain, and now pass to the study of the conditions in the spinal cord. That "hindbrain neuromeres" could be compared with segments of the spinal cord was an afterthought on the part of embryologists, evidently born of the conception that the head has a segmentation comparable with that in the trunk.

While the neural plate in the trunk region is still widely open, its dorsal surface exhibits cross furrows, which are proved by longitudinal sections to correspond with the interspaces, or clefts, between the mesodermic somites. The number of the cross furrows exactly equals that of the interspaces, increasing in number as the constrictions between the somites do. They do not, however, extend to the edges of the neural plate, but are restricted to the region where the plate rests upon the somites. In these cross furrows we have the first indications of those structures which were called by McClure ('89) "myelomeres," and were

compared by him with the "neuromeres" of the medulla.¹ Such symmetrical cross furrows on the widely expanded neural plate of embryos of *Salamandra atra* were described by Kupffer ('86), and considered by him as remnants of a primitive segmentation. Since Kupffer believed that at this stage there was no trace of mesodermic somites, he regarded the segments as "primary," i. e. not formed secondarily in adaptation to the mesodermal segmentation. Both Froriep ('92) and Wiedersheim ('92) have, however, declared that mesodermal somites are present at the stage described by Kupffer, and that the segments could be explained as the passive result of the pressure of these somites. Locy ('95) finds in the trunk region of embryos of *S. acanthias* with a widely expanded cephalic plate that the lines of division between his "neural segments" may be traced inward toward the median furrow, probably as the result of the appearance of somites in that region. As stated on page 160, I have failed to find this exact correspondence between the neural segments of Locy and the somites.

When the neural plate has closed to form the neural tube, the regions of elevation between the furrows become constrictions, which however affect only the ventral half of the tube, i. e. that portion against which the somites lie (see Fig. 41, Plate 6). Neither frontal sections nor cleared specimens give evidence of constrictions in the dorsal half of the tube. The constrictions in the ventral half of the tube are most clearly marked in the early stages, when the mesodermal somites are most rounded in form, and they disappear as this rounded form disappears.²

Figure 39, Plate 6, represents a frontal section in the ventral half of the myelon of an embryo with 28-30 somites (Balfour's stage H). The right half of the neural tube and of the mesoderm is shown. It is seen that the wall of the neural tube shows a rounded constriction opposite the somite, while opposite the cleft between two somites, and conforming with it, an outer ridge and an inner rather sharp groove are seen. This section affords evidence more favorable to the contention that "neuromeres" exist in the spinal cord than that seen at any other stage of development, or in any other plane of sectioning. In dorsal sections of the same series the constrictions disappear, as do the somites also.

¹ Marshall ('78) had previously stated that in the chick "the cord is slightly constricted opposite the centres of the protovertebræ, and slightly dilated opposite the intervals between successive protovertebræ."

² Miss Platt ('89) has said with regard to the chick, "Here [in the trunk region] as in the medulla, the segmentation is more manifest in the ventral region than in the dorsal."

The structure of the myelomeres in embryos of 40-50 somites is represented in Figures 42 and 43, Plate 6. As in Figure 39, only the right half of the embryo is shown. The only evidence of the structural peculiarities of neuromeres at this stage consists in an external constriction opposite the myotome and the spinal ganglion (Fig. 43). In sections dorsal or ventral to the one shown in Figure 43, even this constriction becomes lost (see Fig. 42, which is more ventral, occupying the region of the ventral roots). All traces of an internal dilatation and constriction, and of the concomitant radial arrangement of cells, have disappeared. In the head, on the contrary, the "neuromeres" still preserve all the characteristics seen in the earlier stages.

An examination of the structure of the myelomeres shows that the conditions are easily explicable on the mechanical grounds stated. There are no serial thickenings of the wall of the neural tube, as in the hindbrain, and the radial arrangement of cells and nuclei shown in the frontal sections (Fig. 39) presents no difficulty; for the cells composing the epithelium of the neural tube always have their long axes perpendicular to the surface of the tube, so that, if the tube becomes constricted opposite each somite, the cells will necessarily show a radial arrangement in frontal sections. In view of this fact, it is difficult to understand how investigators should have thought that the existence of a radial arrangement of cells and nuclei was evidence sufficient to establish the morphological value of myelomeres, and their serial homology with hindbrain neuromeres. McClure ('90), for example, says, "The lateral walls of the spinal cord are divided into neuromeres which, while less conspicuous, have all the cellular characteristics seen in the typical neuromeres of the hindbrain, and in fact are a continuation of the latter." That all of the cellular characteristics seen in the typical neuromeres of the hindbrain are also found in the myelomeres is demonstrably untrue for *Squalus*, as may be seen by comparing the sections shown in Figures 38 and 39, Plate 6, both from the ventral half of the neural tube of the same embryo, one in the head and the other in the trunk. The cellular arrangements are decidedly unlike. In the head (Fig. 38) the cells and nuclei are crowded in the region of constriction between neuromeres, while in the trunk, if the cells are crowded at all, it is in the region of dilatation of the myelomere.

It has seemed a strong argument for the serial homology of myelomeres and hindbrain neuromeres that the former continue into the latter gradually and in an unbroken series. For example, McClure ('90) stated that "the constrictions of the myelon (in Lizard embryos) gradu-

ally pass or merge into those of the encephalon, thereby forming a continuous series of constrictions throughout the entire length of the neuron, which increase in size anteriorly." Also, in demonstrations of this continuity, Miss Platt ('89) stated (for the chick) that "the difference (in size) between the fifth neuromere [last neuromere of the medulla] and the next posterior fold is not as great as the difference between the second and third neuromeres." (Compare Fig. 44, Plate 7.) Locy ('94 and '95) says of his neural segments that "those in the trunk region are continuous with those of the head, and pass into the latter without any transition forms." Zimmermann ('91), on the other hand, does not find the spinal cord in *S. acanthias* to be segmented.

While I am able to confirm the evidence of continuity of encephalomeres and myelomeres as stated by previous investigators, I am unwilling on this ground alone to regard these structures as of the same morphological value. Moreover, it has been shown that the hindbrain neuromeres and the myelomeres differ both in structure and in development.

b. SUMMARY.

The evidence presented by the constrictions of the myelon warrants the inference that the existence of the myelomeres is dependent upon the presence of the somites, an explanation by no means possible for the hindbrain neuromeres. The constrictions of the myelon appear only after the somites are formed, and increase in number with the addition of new somites. They are opposite the somites, and are confined to that portion of the neural tube against which the somites lie, i. e. the ventral portion. They present no histological or structural conditions which are not easily reconcilable with the hypothesis of their mechanical formation. In those Vertebrates in which the somites extend farther dorsally with reference to the neural tube, the constrictions of the myelon also have a greater dorsal extent. As soon as the somites lose their rounded form and no longer lie close to the neural tube, the constrictions of the tube disappear. As a whole, the evidence in the spinal region of *Squalus* fully confirms the explanation given by Minot ('92), viz. that the appearance of the myelomeric constrictions "seems to depend upon the development of the primitive segments of the mesothelium. When the segments are fully formed, and before their inner wall has changed into mesenchymal tissue, they press against the medullary tube and oppose its enlargement; at least one sees that the tube becomes slightly constricted between each pair of segments and slightly enlarged opposite each intersegmental space." Structurally, therefore, myelomeres and

encephalomeres differ. While a mechanical explanation is possible for the one, such is not possible for the other. They are, it is true, continuous serial dilatations of the neural tube. The proof, however, that they are of equal morphological value, that is to say, serially homologous, rests, I believe, in the demonstration of a similar metameric relation to organs known to be segmental. The myelomeres correspond metamERICALLY with the somites, as has been stated. Do the encephalomeres likewise correspond with somites? Upon the answer to this question obviously depends largely the decision as to their *metameric* value. Before stating the evidence bearing upon this question it is necessary to see if there is any evidence of neuromeres anterior to the hindbrain.

IV. The Neuromeres anterior to the Hindbrain.

a. ESSENTIAL CRITERIA OF NEUROMERES.

I believe that those who find neuromeres in the brain region anterior to the hindbrain have assumed the presence of a homodynamous segmentation of the entire encephalon. Yet it must be admitted that even if a serially homologous segmentation extends from the spinal cord into the medulla oblongata, it by no means follows that such segmentation also extends into the anterior brain region. Compare with the analogous case of the skull. Because the occipital region is segmental, i. e. composed of fused vertebræ, it does not follow that the pre-otic region is. It is well, at least, to study the conditions in the anterior brain region with the mind as unprejudiced by any theory as possible. What criteria, then, warrant the conclusion that any given division of the neural tube is a neuromere? Certainly, no one criterion would be held to be sufficient. The best criteria are such as associate the supposed neuromeres metamERICALLY with other structures known to be segmental, e. g. the mesodermic somites or the segmental nerves. But where such direct evidence is wanting, to say that a radial arrangement of cells and nuclei is evidence of a neuromere, and thus indirectly evidence of a metamere, is obviously dangerous, since the radial arrangement of the nuclei appears whenever the neural tube is constricted from any cause whatever.

If, however, we have rudimentary somites in the head, may we not also have rudimentary neuromeres? McClure ('89) finds between the midbrain and the optic vesicle of the Lizard a structure which resembles a portion of a neuromere, — a "half-neuromere." He accepts the evi-

dence of neuromeres in the primary forebrain also, although the arrangement of nuclei does not always conform to the typical condition. Waters ('91, p. 143) says: "In this area [that of the posterior commissure] the Cod brain shows little or no segmentation, but from the fact that it nearly corresponds in extent to neuromere II, and that its existence is quite evident in *Amblystoma*, it seems probable that this space is occupied by the third and last of the forebrain neuromeres." In other words, though none of the characteristics of a neuromere are present, it is *a priori* probable that a neuromere exists here!

Orr, Béraneck, and Miss Platt have regarded the midbrain vesicle as a single enlarged neuromere. It has an external constriction separating it from its neighbours, a corresponding internal ridge, an inner concavity, an outer convexity, a radial arrangement of cells and nuclei, and in addition is primary in time of appearance. On the other hand, Waters ('92) says that it is an error to confound the neuromeric segmentation with the so called vesicular segmentation, since he finds in the midbrain region "*two*¹ well marked convolutions of the brain wall," and the characteristic radial arrangement of nuclei. Kupffer ('93^a) believes that, since, with Froriep (92^a) and Zimmermann (91), he finds evidence of *three* encephalomeres in the midbrain,² this confirmation gives a certainty to their results.

Surely the divergence in the results of other investigators has not *proved* that Orr, Béraneck, and Miss Platt were wrong in considering the primary midbrain as a single neuromere, especially since the midbrain and forebrain form parts of a continuous series of primary enlargements of the encephalon. The majority of investigators (Orr, Béraneck, McClure, Froriep, and Zimmermann) find that the forebrain consists of *two* neuromeres, without however giving a satisfactory explanation of its marked divergence, in the matter of secondary division, from the typical hindbrain dilatations. If we count dorsal expansions, as is done by Waters and others, we may find evidence of at least *three* neuromeres, which correspond, says Kupffer ('93^a), with his *Grosshirn*, *Nebenhirn*, and *Schalthirn*. Furthermore, if dorsal diverticula be regarded as evidence of neuromeres, we must agree with Kupffer that it is impossible to disregard the epiphyses and plexus formations.³ On this basis

¹ Waters says (p. 465) that he thinks McClure is mistaken in assigning to the midbrain region, on purely speculative grounds, a *third* neuromere.

² Kupffer found these three secondary subdivisions of the midbrain in *Cyclostomes*, Zimmermann in *Selachii*, and Froriep in *Mammalia*.

³ See Kupffer ('93^a, p. 549).

Kupffer finds at least *five* encephalomeres in the primary forebrain. This conclusion seems strengthened by the conclusion of Burckhardt ('93), that the median zones of the neural tube retain throughout the Vertebrate series the primitive segmentation best, and therefore are the best for comparison.

My conclusions from a study of the evidence presented by those who have assumed a segmental value for the secondary subdivisions of the forebrain and midbrain vesicles are, (1) that morphologically different structures have been described by them as "neuromeres" or "encephalomeres," and (2) that the divergence in their results does not seem to justify this assumption.

I now turn to an examination of the development of forebrain and midbrain regions in *S. acanthias*, in order to determine whether or not it is probable that structures morphologically comparable with hindbrain neuromeres exist in these regions. Since hindbrain neuromeres involve all three zones—dorsal, ventral, and lateral—of the walls of the encephalon, the value of forebrain and midbrain segments as morphological equivalents of them will clearly depend on their similarly involving those zones. If they do not, it is incumbent upon one who holds to their equivalency to demonstrate how modification has probably obscured or obliterated the primitive conditions. Evidence in such a highly specialized region can be at best only probable. Here, however, as always, the demonstration of morphological comparability must be "controlled" by the demonstration of similar relationships to other organ systems.

5. DEVELOPMENT OF THE FOREBRAIN AND MIDBRAIN.

At a stage with 19 or 20 somites the conditions in the anterior brain region are very simple. The primary forebrain and midbrain are simple vesicles or enlargements of the neural tube.¹ A parasagittal section cut through the right wall of the neural tube is represented in Figure 45, Plate 7. Six vesicles are counted, all of them being included in the region of the cephalic plate. The anterior vesicle shown is the wall of the forebrain in the region of the optic vesicles. Behind lies the midbrain, separated by a slight constriction from that region of the hindbrain to which Zimmermann ('91) has given the name "Hinterhirn."¹ Hindbrain neuromeres IV, V, and VI are clearly defined.

A frontal section of an embryo of the same stage, so cut as to coincide

¹ The English term hindbrain has been applied to the region separated by the Germans into "Hinterhirn" and "Nachhirn."

with the axis of the midbrain vesicle, is shown in Figure 49, Plate 7. The vesicle of the primary forebrain (I) appears as an almost circular enlargement of the anterior portion of the neural tube. Behind this, and separated from it by a constriction, lies the narrower and somewhat more elongated midbrain vesicle (II). Posteriorly a small portion of the "Hinterhirn" vesicle also appears in the section.

Sagittal sections of embryos at this stage are seen in Figures 8 and 9, Plate 3. Faint dorsal constrictions separate forebrain, midbrain, and "Hinterhirn" (III), the separation between midbrain and "Hinterhirn" being very slight. A deep depression in the floor of the forebrain marks the position of the infundibulum, which is bounded posteriorly by a faint constriction, the first indication of the tuberculum posterius (Kupffer). Another constriction of the ventral wall of the neural tube is seen behind the tuberculum posterius in the region of the midbrain, — the plica encephali ventralis. In later stages the region of this constriction becomes the point of greatest flexure of the neural tube. The constrictions marking off the brain vesicles appear as rather broad depressions, not sharply defined as are the constrictions between neuromeres. The brain vesicles are also seen to be considerably larger than the hindbrain neuromeres, the difference in size constantly increasing from this stage onwards. Except for a local thickening of the lateral zones, the two anterior brain vesicles are structurally quite comparable with the hindbrain neuromeres. They similarly involve all three zones of the neural tube.

An examination of embryos at a stage with 28 to 30 somites, i. e. early in Balfour's stage H, shows that slight changes have occurred. A parasagittal section of such an embryo is shown in Figure 46, Plate 7. The anterior vesicle, the forebrain, is so cut that one sees its lumen. Behind this, and separated from it by a constriction which extends to the ventral portion of the tube, lies the midbrain, which dorsally is a single expansion passing almost without constriction into the hindbrain. The depth of the constriction is much less than it appears to be in this figure, because the section passes to one side of the median plane. In the ventral half of the midbrain there is a constriction, which more median sections of this stage (Fig. 13, Plate 3) show to correspond with the region of sharpest flexure of the neural tube (plica encephali ventralis). This constriction does not extend, however, to the dorsal portion of the neural tube, and therefore is not equivalent to a constriction which separates neuromeres. By it the midbrain is separated ventrally into two lateral expansions on each side of the head, — one

anterior, the other posterior, — while dorsally it remains a single dilatation. The anterior of the two expansions narrows as it extends ventrally, and terminates at a point in the ventral wall near, but anterior to, the tuberculum posterius. The posterior of the two midbrain expansions is bounded behind by the faint lateral constriction between midbrain and hindbrain vesicles.

The conditions shown in a sagittal section at this stage are not essentially different from those presented at the stage previously described (Fig. 13, Plate 3). The forebrain, midbrain, and "Hinterhirn" vesicles are separated by very faint dorsal constrictions. In the constriction between forebrain and midbrain vesicles appears later Miss Platt's "thalamic nerve." Ventrally two constrictions are seen, one corresponding with the tuberculum posterius, and the other, more posterior, with the point of greatest flexure of the neural tube. Two frontal sections of an embryo at this stage are shown in Plate 7, Figures 48 and 50. Figure 48 represents the more dorsal of the two, and shows only the expansion of forebrain and midbrain vesicles separated by the primary constrictions spoken of above. A small portion of the "Hinterhirn" is shown. The section shown in Figure 50 is more ventral, being in a plane about midway between the dorsal and ventral sides of the neural tube. An arrow is drawn at the constriction separating forebrain and midbrain vesicles. This constriction corresponds with the one seen in the more dorsal section, also indicated by an arrow. Behind this, in the region of the midbrain, another constriction appears, one which was not seen in the dorsal section. This may be traced in more ventral sections into the constriction previously described as occupying the floor of the midbrain at a point corresponding with the point of greatest flexure of the neural tube. In my opinion everything in front of the arrow belongs to the primary forebrain, the lateral walls of which are expanded to form the optic vesicles. Behind these two vesicles are seen "two well marked constrictions and two convolutions" of the neural wall which show radially arranged nuclei.¹ It is found in later stages that the posterior of the two constrictions corresponds in position with the posterior commissure, and therefore that what lies anterior to this constriction must be considered as part of the thalamencephalon. It is seen, therefore, that the constriction between primary forebrain and midbrain vesicles does *not* correspond with the posterior commissure, which in later stages forms by common consent the anterior boundary of the midbrain (see

¹ Probably the two "neuromeres" of the thalamencephalon described by Orr ('87).

Plate 7, Fig. 47, *coms. p.*). This constriction corresponds, instead, with a point just behind the epiphysis, and is separated from the posterior commissure by that portion of the brain which Kupffer has named Schalthirn, or diencephalon (the Schaltstück of Burckhardt). Neither of the so called neuromeres (Orr) is in relation with a nerve, motor, or sensor, and neither possesses a dorsal expansion of its own.

A parasagittal section of the next older stage represented is seen in Figure 47, Plate 7 (compare Fig. 19, Plate 4); it is of an embryo with 65 somites (Balfour's stage K), and the changes in the anterior brain region are seen to be considerable. In the dorsal portion of the region called primary forebrain, i. e. the region anterior to the constriction in which the "thalamic nerve" (*thl.*, Fig. 18, Plate 4) lies, two expansions now appear. These are median, unpaired, and separated from each other by a constriction which extends toward, but does not reach, the optic stalk. The anterior expansion is the prosencephalon (Grosshirn, epencephalon of Kupffer), which involves, as determined by His (88*), the "Deckplatte" and both "Flügelplatten." The second, which at this stage is a simple expansion, later becomes differentiated into "Zirbelpolster" (Kupffer's parencephalon, Nebenhirn) and the epiphysis. The latter, according to His, is derived from the "Deckplatte" only. The primary constriction between forebrain and midbrain is marked in Figure 47 by the dorso-ventral line, behind the second expansion. The midbrain now shows three lateral expansions. The anterior is bounded in front by the primary constriction between forebrain and midbrain, and behind, as in the previous stage, by the ventral (and now lateral) constriction which extends dorsad toward the posterior commissure from a point just in front of the chief root of the oculomotor nerve. The second dilatation has as its posterior boundary a ventral constriction which I do not consider of morphological importance, because it simply corresponds with a point of flexure of the ventral wall of the tube, never extends to a dorsal position, and has no corresponding inner ridge. The constriction exists, however, at this stage, and forms the posterior boundary of a neural segment related to the oculomotor nerve. Behind this lies a third expansion, faintly marked anteriorly and also posteriorly, where it merges into the isthmus. In later stages the trochlear nerve arises from the region of the posterior constriction of this expansion; it is the chiasma of fibres of this nerve which defines the posterior constriction of the midbrain vesicle. In this stage, as in the preceding, the midbrain vesicle remains dorsally a simple expansion, the constrictions affecting only its lateral and ventral walls.

Two frontal sections of an embryo at this stage are seen in Figures 51 and 52, Plate 7. Anteriorly in the more dorsal section (Fig. 51) is seen the expansion of the prosencephalon. Behind this lies an expansion which might be considered as a neuromere, if a radial arrangement of nuclei and a constriction of the brain wall were alone considered sufficient criteria for such a structure. Since, however, it is simply a dorsal expansion, which is unrelated to nerves, and soon becomes differentiated into adult organs, I am unable to regard it as a neuromere. From it are differentiated "Zirbelpolster" (parencephalon, Nebenhirn, or Zwischenhirnblase) and epiphysis. Posterior to the constriction marked by the arrow, which corresponds with the point so marked in Figure 50, is situated a long expanded portion of the encephalon which passes without constriction into the midbrain vesicle. In the more ventral section (Fig. 52), however, there is seen in this region a constriction which may be traced ventrally to that point from which the anterior root of the oculomotor arises. Two neuromere-like expansions, separated by the constriction between primary forebrain and midbrain, are seen in this stage as in the previous stage described.

Passing now to a much later stage (21-22 mm.), we find (Plate 4, Fig. 21) that the posterior commissure has come to lie much nearer the base of the stalk of the epiphysis, and thus that the portion of the dorsal wall which is called by Kupffer diencephalon has become much reduced in the region of the midbrain vesicle. Thus it has come about that frontal sections in a plane midway between the dorsal and the ventral walls of the neural tube (Fig. 53, Plate 7) show only a single neuromere-like expansion. In more dorsal as well as more ventral sections this undergoes constriction, so that it is by no means a simple neuromeric enlargement. A median sagittal section, such as that shown in Figure 21 (Plate 4), is the most satisfactory for the study of segmentation at this stage. The primary forebrain is now differentiated into the successive dorsal dilatations epencephalon, paraphysis (parencephalon), and epiphysis. Dorsally the midbrain still continues to be a simple expansion, while ventrally traces of the three segments still remain, the anterior one having become much reduced in length.

With the exception of Locy, Zimmermann ('91) is the only investigator who has studied the "neuromeres" in Selachii. For the purpose of comparison, it is well to state his results here. He finds at first *eight* "primäre Abschnitte" in the encephalon, the first three of which exceed in size the last five. The first three are the Vorderhirn, Mittelhirn, and Hinterhirn, each of which he regards as a complex of en-

cephalomeres, since they later subdivide into segments which dorsally are equally long and broad. The Vorderhirn divides into two encephalomeres, the Mittelhirn into three, and the Hinterhirn into three. Thus, since the posterior five "primäre Abschnitte" do not further subdivide there are in all thirteen "encephalomeres." As a result of cephalic flexure some of the encephalomeres become wedge-shaped, but all are clearly separated from one another by constrictions. Zimmermann's paper was a preliminary one without figures, and it has not as yet been followed by a final paper.

It is seen that Zimmermann's account, based on the study of *S. acanthias* embryos, differs somewhat from my own. At the closure of the neural tube I find six vesicles or expansions of the encephalon. The first three correspond with those called by Zimmermann Vorderhirn, Mittelhirn, and Hinterhirn; the last three are hindbrain neuromeres IV, V, and VI. Since Zimmermann's 7th and 8th "primäre Abschnitte" are not differentiated at this stage, I am unable to accept his conclusion that there are at first *eight* primary "encephalomeres" or "Abschnitte." The primary forebrain subdivides into the two dorsal expansions which Zimmermann calls "Secundäre Vorderhirn" and "Zwischenhirn." But, if these are "encephalomeres," I am unable to see how later differentiations, such as the prosencephalon (epencephalon), paraphysis (parencephalon), and epiphysis can be excluded from the same category. May we not have tertiary as well secondary "encephalomeres"? I am unable to accept Zimmermann's single criterion of size as sufficient to enable us to make a distinction between those segments which are primitive, i. e. remnants of ancestral structures, and those which are the early beginning of adult organs. A most serious objection to regarding such structures as Zimmermann's "Secundäre Vorderhirn" and "Zwischenhirn" morphologically comparable with neuromeres or myelomeres has been stated by Herrick ('92), and consists in the difficulty of homologizing dorsal expansions with ventral ones.

The primary midbrain, as stated by Zimmermann, subdivides into three segments, the most anterior of which lies in front of the posterior commissure and in front of the place of origin of the oculomotor nerve. In all stages the midbrain is seen in median sagittal sections to present a simple dorsal expansion, its constrictions affecting its ventral and lateral walls only.

The third vesicle, Zimmermann's Hinterhirn, which he says subdivides into three "Encephalomeren," I find to become differentiated into the cerebellum Anlage and a posterior enlargement or thickening, but nothing

more. The only evidence which I find of Zimmermann's anterior "Hinterhirn Encephalomer" consists of a flexure of the median ventral wall appearing in late stages in the anterior portion of the Hinterhirn. Since no dorsal or lateral constriction corresponds with this, and since therefore it cannot be regarded as a vesiculation of the neural tube, I do not consider it as of morphological importance, but explicable simply as a passive result of the flexure of the neural tube.

Locy ('95, p. 542) finds five "neural segments" in the forebrain and midbrain, — three in the former and two in the latter. He clearly figures and mentions in the description of plates, however, the three secondary midbrain expansions described by Zimmermann and myself.

c. SUMMARY.

An examination of the literature bearing on the question of neuromeres in the region anterior to the hindbrain had led me to the conclusion that structures of different morphological value had been described as neuromeres, and the examination of the secondary subdivisions of the forebrain and midbrain of embryos of *S. acanthias* has served to strengthen this opinion. These subdivisions have been shown to differ from the typical neuromeres in shape, in structure, and in relation to the dorsal and ventral zones of the neural tube. The attempt to establish a serial homology on the basis of such structures alone seems to me quite misleading; not less so, indeed, when we attach hypothetical nerves (dorsal, lateral, and ventral roots) to them.

Moreover, the late appearance of the so called neuromeres of the anterior brain region, together with the fact that they are secondary subdivisions of primary vesicles, and thus differ from the hindbrain and spinal expansions, seems a serious objection to the contention that they afford satisfactory evidence of a primitive metamerism. Zimmermann ('91) attempted no explanation of this difficulty, saying merely that the differentiation of the anterior encephalomeres is *retarded* for reasons unknown to him. Waters ('92) alone offers an explanation. To him it seemed "not unreasonable to conjecture that these constrictions, being essentially primitive and in a state of degeneration, have gradually been more and more crowded out by the specializing brain development, and hence appear at a much later period in the ontogeny than would be expected." What right, we are tempted to ask, has one to *assume* the primitive nature of "forebrain neuromeres," in view of the *facts* that they are late differentiations, and that some of them are the fundamentals of adult organs, and in this respect differ both from the typical hindbrain neuromeres and

from the expansions of the myelon? Every fact which we possess seems to me to argue against their primitive nature. In my opinion the assumption of Herrick ('92), that, "if neuromeres once existed in the forebrain, they would be visible only at an early stage, and would be obscured by altered conditions," is the more reasonable of the two assumptions. On the basis of structure and of relation to other segmentally arranged organs, however, I conclude that the primary vesicles, the forebrain and midbrain, give evidence — as do the primary expansions of the hindbrain — of the primitive segmentation of the Vertebrate head. I now turn to an examination of these relations, first, to those of neuromeres and somites, since they are the most important.

V. The Relation of Neuromeres to Somites.

a. RELATION OF MYELOMERES TO SOMITES.

Since the myelomeres, as has been stated, show a definite (numerical) correspondence with the trunk somites, the expansions of the spinal cord alternating with the somites, it is evident that proof of the serial homology of myelomeres and encephalomeres will rest very largely on the demonstration of a similar correspondence of the latter with head somites, if there be such. Yet, so far as I know, Miss Platt is the only investigator who has affirmed that there is such correspondence for the head region. She writes ('91, p. 82) as follows: "The line of somites [in *Squalus*] alternating with the neuromeres is continued into the head as far forwards as the alimentary pocket which is to form the second visceral cleft. Here complete divisions of the mesoderm cease, but serial depressions in its dorsal wall indicate incomplete divisions into three parts above the hyoid arch (van Wijhe found *two* somites here) and two parts above the mandibular arch [van Wijhe found *one* somite here]. Like the somites of the trunk, the divisions thus marked off alternate with the neuromeres, lying opposite successive constrictions of the brain. The anterior division of the mandibular cavity corresponds to the constriction that separates the midbrain from the hindbrain, or to that from which the trochlear nerve arises." The same investigator likewise says in regard to *Necturus* ('94, pp. 960, 961): "Hinter der Hyomandibularspalte wechseln die primitiven Neural- und Mesoderm-Segmente regelmässig mit einander ab. Die mesentodermale Segmentation ist dieselbe, die von v. Wijhe den Selachiern zugeschrieben wird."¹

¹ It is seen that Miss Platt finds the segmentation, both neuromeric and mesomeric, different in *Squalus* and *Necturus*. While in embryos of the former she

b. RELATION OF ENCEPHALOMERES TO SOMITES.

With Hoffmann ('94 and '96) I am able to confirm the presence of van Wijhe's head somites in *Squalus* (*Acanthias*) and also Platt's "anterior" somite. Valuable as this repeated confirmation appears to me, I regard as equally important the fact that anterior to the sixth (van Wijhe's) somite *a mesodermal segment corresponds to each of the primary encephalic vesicles* (encephalomeres I to VII). A topographic alternation, however, such as that affirmed by Miss Platt for the hindbrain region of *Squalus* and *Necturus*, I do not find. In the early stages of development van Wijhe's sixth somite lies opposite the posterior constriction of encephalomere VII, but this relation is soon lost. However, the numerical correspondence seems important, and I believe that it will be shown by a study of nerve relations that the correspondence is not without morphological significance.

c. SOMATIC VALUE OF THE PRE-OTIC MESODERM SEGMENTS.

Although it has been stated that the purpose of this paper is to discuss the nature of the neuromeric segmentation and the relations of neuromeres to other segmental structures, it seems to me not inconsistent with this purpose to inquire into the credentials of those mesodermal segments in the Selachian head which van Wijhe in his famous paper considered of somatic value. The confirmation of their presence in *Squalus* given by Hoffmann ('94 and '96) and myself ('96), while strengthening the belief in their permanency, which has been greatly shaken by the discovery of more numerous segments in other Selachii (*Torpedo*), by no means demonstrates their somatic value.² The dis-

finds in the hindbrain region two more somites than were seen by van Wijhe ('82) and a numerical correspondence of these with the neuromeres, in the latter, on the contrary, she finds neuromeres corresponding with a somatic segmentation which is the same as that found by van Wijhe. She finds, therefore, it may be inferred, two less hindbrain neuromeres in *Necturus* than in *Squalus*. In embryos of *Amblystoma* I find, in agreement with McClure ('90), no neuromere corresponding with encephalomere IV of *Squalus*, i. e. there is one less neuromere in the Urodele than in the Selachian. Now, since I find a numerical correspondence of van Wijhe's somites with hindbrain neuromeres (encephalomeres III-VII) in the Selachian, it is clear that they could not likewise correspond in the Urodele. However, I have been unable to find evidence of pre-otic somites in *Amblystoma*, and therefore am unable to affirm or deny a correspondence of neuromeric and mesomeric segmentation in this form.

² It is a matter of great interest that the latest investigation upon *Torpedo* (Sewertzoff, '98) shows that the mesodermic segmentation in *Torpedo* and *Pristiurus* is the same. Thus van Wijhe's results receive repeated confirmation.

crepancy in the results of investigators of the mesomeric, as well as of the neuromeric, segmentation most certainly justifies Rabl's ('89) complaint of the hasty way in which investigators have given mesodermal segments somatic value. In no question of morphology to-day is conservative judgment more needed. Before stating my own evidence I will briefly summarize the arguments advanced by previous investigators for and against the somatic value of the mesodermal segments of the head.

(1) In addition to the evidence first stated by Marshall ('81), that the dorsal mesoderm of the head of Selachian embryos undergoes a segmentation independent of the segmentation of the visceral arches, van Wijhe ('82, p. 4) uses the following arguments for the somatic value of his somites : "(2) Dass die Länge der Somite sich im ganzen Körper gleich verhält. (3) Dass die obere Grenzlinie der Rumpfsomite ununterbrochen in diejenige der Kopfsomite übergeht. (4) Dass die untere Grenze der Somite sowohl im Kopfe als im Rumpfe nur wenig unter der oberen Grenze des Darmes liegt." The latter proof has been amplified by Killian ('91) from the evidence that the head somites are dorsal in relation to chorda, dorsal aorta, and epibranchial (medio-lateral) line. (5) Hoffmann ('94) and Miss Platt ('97) have confirmed van Wijhe's statement that the development of the somites begins in the neck region and proceeds continuously both posteriorly and anteriorly. Furthermore (6) the same constituent parts, viz. myotome and sclerotome, may be distinguished in the head as well as in the trunk somites (van Wijhe, '82, Killian, '91). To this Miss Platt ('91) adds (7) the evidence that, as in the case of the somatic musculature of the trunk, the muscles derived from the "anterior," the first, the second, and the third somites (rudimentary in the case of the anterior and somewhat modified in the case of the first somite) first appear in the median wall of these somites. Finally (8) there is a correspondence of the neuromeres and mesodermic segments throughout the entire length of the neural tube (Neal, '96).

The following are the arguments advanced in opposition to the somatic value of the mesodermal segments of the head.

(1) The divisions of the mesoderm of the head are due to the mechanical influence of the neighboring parts, chiefly that of the visceral pouches (Kastschenko, '88).

(2) The divisions are irregular in size (Kastschenko, '88, Rabl, '89).

(3) In van Wijhe's third proof there is "nicht die Spur eines Beweises für die Richtigkeit seiner Ansicht" (Rabl, '89, p. 234).

(4) The 1st somite is an exception to van Wijhe's fourth argument (Rabl, '89); moreover, the constrictions are never complete in the case

of the somites 2 to 5 (Katschenko, '88, Rabl, '89), so that it is impossible to state the position of their lower boundary with reference to the dorsal wall of the alimentary canal (Rabl, '89).

(5) The development of the "head cavities" is discontinuous with that of the trunk somites (Rabl, '89, Kupffer, '93). While the development of the pre-otic segments takes place later than that of the trunk somites, the differentiation of mesenchyma takes place much earlier in the head than in the trunk. This conflicts with the law, that in the Anlagen of serially homologous organs the older the Anlage the earlier the histological differentiation (Rabl, '89).

(6) There never appears in the case of the pre-otic segments a differentiation into myotome and sclerotome (Rabl, '89, p. 235).

(7) While the musculature of the trunk and occipital somites arises exclusively from the median wall of the somite, the musculature of the pre-otic segments has its origin in greater part from the lateral, and in smaller part from the posterior wall of the so called somites.¹ Moreover, while only a distinct and sharply defined portion of the trunk somites proliferates mesenchyma, the entire median wall of the pre-otic segments participates in the formation of mesenchyma (Rabl, '89).

(8) The topographic relations of the dorsal nerves in later stages are different in head and trunk. In the head the nerves grow laterad to the somites, while in the trunk they grow mediad to them (Rabl, '89).

Special arguments, in addition to the general ones stated above, concerning the nature of the anterior, the 1st, and the 2d mesoderm segments have been made, because of their marked peculiarities in development, structure, and relations, and of their important bearing upon the question of the morphology of the eye muscles. It will therefore be necessary to state these also.

Two chief opinions concerning the nature of the anterior (Platt's) and the 1st and 2d (van Wijhe's) mesoderm segments are now held: (1) that they are serially homologous with trunk somites (van Wijhe, Platt, Hoffmann, Neal, Fürbringer); (2) that they are abortive visceral pouches (Kupffer, '88, Froriep, '92, Sewertzoff, '95). The discussion, therefore, turns upon the question whether these structures represent diverticula (dorsal) of the mesoderm, or lateral diverticula from the alimentary canal.

Miss Platt ('91, '91a) argues for the somatic value of the anterior somite (cavity) as follows:—(1) In position, independence, and time of origin this cavity resembles the following ones. (2) Many cells from its

¹ Balfour ('81) holds that both median and lateral walls of the trunk somites form the lateral trunk musculature.

median wall migrate into the centre of the cavity, and cells bounding the inner wall above and below assume the elongated contour of muscle cells.

Hoffmann ('94, p. 649) also, while not able to state with definiteness that the anterior cavity is a dorsal or lateral diverticulum from the alimentary canal, i. e. whether it represent a mesoderm segment or a visceral pouch, considers it probable that it represents the former, since it is very similar to the succeeding head cavities of van Wijhe. Hoffmann mentions the migration of cells into the cavity of the somite, but does not specify from which wall they are proliferated. He also states that from the walls of the somite "entstehen keine Muskelfasern" ('96, p. 256). Against these views of Miss Platt and Hoffmann no special arguments have as yet been raised.

The first somite of van Wijhe possesses the peculiarity of a median stalk connecting the somites of the opposite sides of the body.¹ The relations of this stalk to the dorsal wall of the alimentary canal, to chorda, and to dorsal aorta have been used as the chief criteria in contending for its dorsal or its ventral nature. The evidences that the first somite represents somatic (dorsal) mesoderm are as follows: (1) Its cells are proliferated from the dorsal wall of the alimentary canal (Platt, '91).²

¹ Such a median connection, however, also appears in the early stages of development of the "anterior cavities." The connecting stalk of the "anterior cavities," however, as stated by Hoffmann, never possesses a lumen, as does the median connecting stalk of the premandibular cavities.

² Miss Platt, in her earlier paper ('91, p. 81), states that the mesoderm of the premandibular cavity is formed, at least in part, by a proliferation of cells from the mandibular cavity, while in her later paper ('91, p. 256) she writes, "The most anterior mesoderm of the head does not take its origin from the mesodermic plates, but from the dorsal wall of the alimentary canal. The mesodermic plates end with the mandibular cavities." The lumen of the connecting stalk, according to Miss Platt, is, as stated by Marshall ('81), formed secondarily by the fusion of a median with the two lateral cavities. This evidence is interesting, since it bears on the question whether the cavity of the connecting stalk is to be regarded as a part of the archenteron, and would seem to answer this question in the negative. Killian ('91, p. 102), however, finds the connecting stalk a "Sklerotomkommissur," and thus, it is to be inferred, the lumen of the stalk, which according to his account is formed secondarily, not a part of the archenteron. He states (p. 102): "Erwähnt sei noch, dass zwischen den beiden ersten Mandibularsomiten vor dem vorderen Chordaende und über dem Aortensinus ein Mesodermzellenhaufen liegt, der die Sklerotomantelle beides Somiten in Verbindung setzt (Sklerotomkommissur). Was nun der Oralzone angeht, so entsteht sie dadurch, dass die vordersten Zipfel des ursprünglich schwalbenschwanzförmig endenden dorsalen Mesoderms die vordere Darmkuppe (vordere Ektodermtasche von Petromyzon nach Kupffer) über- und umwachsen, und so einen medianen Zellkomplex bilden, aus dessen hinterer

(2) Its connecting stalk is axial in position (van Wijhe, '82); dorsal to carotis (Dohrn, '88). (3) This section of the head cavity is so similar to the remaining sections, that it must be considered as serially homologous with them (Balfour, '81). Oppel ('90, p. 623), however, states (for *Anguis*) that "nur der histologische Bau und die Art der ersten Entstehung dieser vorübergehend im Mesoderm auftretenden Somiten gestattet, an der Deutung festzuhalten dass es sich hier in der That um Somiten handelt."

That the 1st cavity is ventral would seem to follow from the evidence that (1) it arises as an entodermic diverticulum from the prechordal portion of the alimentary canal (Seessel'sche Tasche), whose cavity is at first continuous with that of the alimentary canal (Kastschenko, '88, Kupffer, '88, '90, '93). "Streng genommen," says Froriep ('92*, p. 589), "konnte es übrigens immer noch eher ventral, als dorsal genannt werden, wenigstens was sein Lumen und seine untere Wand anlangt. Denn das Aequivalent der Chorda, welche als Achsenfaden dorsale und ventrale Gebilde scheidet, ist selbstverständlich nur in der oberen Wand des medianen Verbindungsstückes zu suchen."¹ (2) The method of separation of the premandibular head cavity from the entoderm, as well as the presence of a median connecting stalk, serves to distinguish this from the following mesoderm segments (Kupffer, '93). (3) According to Kupffer ('94) the connecting stalk of the premandibular cavity is

Hälfte für jede Seite ein Somit entsteht (van Wijhe's erster), während die vordere Hälfte zu Grunde geht." It is readily seen that this evidence tells decidedly against the view that the connecting stalk is ventral, and against the view of Kupffer and Froriep, that its lumen is a part of the archenteron.

Furthermore, Goette ('90) has given evidences concerning the method of formation of the anterior mesoderm in *Ammocetes* which stands in direct contradiction with that stated by Kupffer, and, if true, takes away the chief support of the theory of the visceral-pouch nature of the anterior mesoderm in that animal. Goette writes: "Unbedingt muss ich aber die angeblichen 'Coelomdivertikel' des Urdarms im Kopf und Vorderumpf für täuschende Bilder erklären, was sich am Besten versteht, sobald man die Mesodermbildung durch die ganzen Schnittserien von vorn nach hinten verfolgt und dabei die vollkommene Uebereinstimmung derselben in allen Regionen antrifft. Ein Blick auf die Abbildungen lehrt, dass von einer verschiedenen Auffassung derselben nicht die Rede sein kann: giebt es im Rumpf keine Coelomdivertikel, so fehlen sie auch im Kopf. Auch die beiden 'präoralen Kopfhöhlen' sind weiter nichts als das erste Mesomerenpaar, welches allerdings wenn man seine erste Anlage in unmittelbarer Fortsetzung der folgenden Mesomeren übersah, später eine Ausstülpung des Urdarms vortäuschen kann, wie ich es weiter oben auseinandersetze." Goette's figures, especially Figures 42, 43, and 44, strongly support his statements.

¹ Willey ('94, p. 175) accepts Kupffer's and Froriep's conclusions.

ventral to the dorsal aorta.¹ The vessel which Dohrn ('88) called the *carotis*, and which he stated lay ventral to the connecting stalk of the first cavity, if comparable at all, is comparable only to the *carotis ventralis* of Amniota.²

The chief arguments concerning the nature of the 2d (mandibular) cavity have already been given in connection with the general question of the pre-otic mesodermal segments, and it is therefore not necessary to repeat them here. The evidence of a continuous lumen between this cavity and the alimentary canal stated by Miss Platt ('91*) has been interpreted by her as favoring the view that the cavity is formed as an outgrowth from the dorsal wall of the alimentary canal, similar to the mesodermal pouches in *Amphioxus*. Kupffer ('94), however, regards it as evidence in favor of his view, that these cavities are abortive visceral pouches. It is necessary, finally, to recapitulate a point in evidence which has only an indirect bearing on the question of the somatic value of the 1st, 2d, and 3d cavities, but which concerns vitally the morphology of the eye muscles (derived in *Selachii* from these cavities). It has been stated by Hatschek ('92) and Kupffer ('92-'96) for *Ammocoetes* (*Petromyzon Planeri*). Their results tend to show that the eye muscles of that low Vertebrate are, with the possible exception of the *musculus rectus posterior* (*externus*), derived from splanchnic and not from somatic mesoderm. According to Hatschek ('92), the *musculus obliquus superior* appears as a differentiated portion of the muscles of the velum, which correspond with the *musculi adductores mandibulæ*. His evidence (pp. 149, 150) is as follows: "Vom vorderen inneren Rande dieses Muskels [velar muscle] dringt nämlich ein Muskelfaserbündel dorsal in das Bindegewebe ein und zieht seitlich am Trabekel vorbei zwischen dem ersten und zweiten Trigeminusganglion hindurch bis in die Nähe des Auges, wo es im Bindegewebe zugespitzt endet. Von da beginnt — wie ein zweiter Muskelbauch — mit seinem zugespitzten hinteren Ende der *musculus obliquus superior* und zieht, wieder anschwellend, in gleicher Richtung weiter zum Auge. Die histologische Uebereinstimmung beider

¹ Kupffer's statement applies to that cavity in *Ammocoetes* which has been homologized, in my opinion correctly, by most investigators (Balfour, Dohrn, Shipley '87, Kupffer) with the premandibular cavity of *Selachii*.

² In my opinion those writers who have quoted Balfour ('81) and Marshall ('81) as holding that the connecting stalk of the premandibular (1st) cavity is ventral have misunderstood them. They both spoke of the two lateral parts of this cavity as prolonged ventralwards to meet below the base of the forebrain. They give no proof that the stalk is morphologically ventral, and in my opinion speak of it as ventral only with reference to the wall of the brain.

Muskelteile ist eine vollkommene. Dieses Verhältnis ähnelt in hohem Grade jenem, welches van Wijhe als ein embryonales von den Selachiern abgebildet hat. Seine Deutung ist aber darin zu korrigieren, dass der m. obliqu. sup. nicht dem parachordalen Muskelblatte, sondern den Seitenplatten zugehört. Die übrigen Augenmuskeln, die in Form eines Kegelmantels an der medialen ventralen Seite des Augapfels sich finden, bilden in Bezug auf ihre Lage und histologische Beschaffenheit eine dritte Gruppe, deren Ableitung nicht ganz sicher erscheint. Sie sind wahrscheinlich von den Konstriktoren des Visceral-apparates abzuleiten. Keinesfalls können sie nach ihre Lage, Verlaufsrichtung und Struktur zu den Seitenrumpfmuskeln in Beziehung gebracht werden."

Kupffer's ('94) results are essentially a confirmation of those of Hatschek. Finding that the premandibular cavity entirely disappears, and that its cells contribute in no part to the formation of the eye muscles, Kupffer is led to doubt the conclusions of those investigators who derive the muscles innervated by the oculomotorius from the epithelium of this cavity. According to Kupffer all the eye muscles (with the possible exception of the musc. rectus posterior) are derived from two visceral arches, the "trabecular" and the mandibular. This evidence, as well as that given by Hatschek, obviously stands in direct contradiction to the somite theory. I am, however, after my study of the literature, inclined to be optimistic concerning the ultimate settlement of the question as to the somatic value of the pre-otic mesodermal segments, for the differences of opinion are not due to equivocal evidence, but to directly contradictory and equally positive statements. We have chiefly to determine who has stated the facts correctly in order to determine whether we shall accept the opinion of van Wijhe, or that of Kastchenko, Rabl, and Frioriep. The evidence obtained by me, which leads me unhesitatingly to accept the view of the first, that the head somites are serially homologous with trunk somites, is as follows. I find the pre-otic mesodermal segments as described by van Wijhe ('82) most clearly defined by mesodermal constrictions or clefts in embryos of *Squalus* with 28 or 30 somites (Plate 3, Fig. 13, Plate 6, Fig. 40, Plate 7, Fig. 46).¹ They are so distinctly marked that they may be seen in whole specimens properly cleared, as well as in sections. Moreover, they are found to be the same on both sides of the embryo.²

¹ Van Wijhe's post-otic mesoderm segments have indisputable somatic value, and need not be brought into discussion.

² An examination of some finely preserved embryos of *Torpedo ocellata*, kindly given me by my friend, Professor A. N. Sewertzoff, leads me to agree with Sedg-

The contention that the constrictions between van Wijhe's somites are incomplete does not appear to me to militate greatly against the view that they have morphological value, inasmuch as their permanency has been repeatedly attested (van Wijhe, Hoffmann, Neal, and Sewertzoff). Nor does Rabl apparently consider this argument as of great weight, since he regards van Wijhe's 5th (1st post-otic) somite — though the constrictions which are found in front and behind are incomplete — as a true somite. The reduction in the myotomic portion of the dorsal mesoderm accounts in great part for the incompleteness of the constrictions. I believe that one who follows the development of the pre-otic and sub-otic mesoderm in *Ammocoetes*, and observes the ontogenetic dissolution of the compact dorsal mesoderm into loose mesenchyma, which follows the great enlargement of the nerve ganglia and of the otic capsule, is in a position to understand the reduction of the dorsal mesoderm in this region in Vertebrates higher in the phylogenetic scale than *Ammocoetes*.¹

wick ('92), that this is not true of the mesoderm segments discovered by Dohrn ('90, '90*) in that form. Dohrn apparently did not endeavor to ascertain whether they were symmetrical or not. I am unable to determine, even in carefully made reconstructions of well oriented frontal sections of embryos at the same stage of development as that described and figured by Dohrn ('90*), whether or not there is a correspondence of the mesodermal segments on the two sides of the head anterior to the one which, in my opinion, corresponds with the 15th segment of Dohrn. While my own negative conclusions cannot be regarded as in any sense disproof of the segmental value of Dohrn's somites, it is my opinion that the evidence of their variability shown by the conflicting results of Killian ('91) tends to throw considerable doubt upon it. Since Killian ('91, p. 108) finds that of the anterior of these segments one is to be regarded as the sclerotome portion of a somite, while others are simply vesicular enlargements of the mesoderm of the mandibular arch, it is to be inferred that Dohrn subjected the head somites of *Torpedo* to little critical examination. To regard as evidence of somites all vacuolar spaces in the dorsal (and lateral!) mesoderm which appear between the somatopleure and splanchnopleure at the time these layers separate, seems to be too uncritical. Similar phenomena appear in the mesoderm of *Squalus* in those early stages of development, when the coelom is in the process of formation, viz. in stages when the neural plate is widely expanded and the embryo possesses 4 or 5 somites. Recent studies by Sewertzoff ('98) render still more doubtful the results of Dohrn and Killian.

¹ A mechanical explanation of the constrictions between the head somites of van Wijhe, such as that offered, but without evidence, by Kastschenko ('88), seems hardly worthy of consideration. That such constrictions as those, for example, between somites 3 and 4, and 4 and 5, cannot result from the so called mechanical influence of visceral clefts, follows from the evidence already stated by Hoffmann ('94 and '96) that in *Squalus*, the constrictions lie dorsal to the visceral arches. I cannot, however, agree with Hoffmann that we may conclude from this evidence that the visceral arches are intersomitic in position, as are the ribs in the

The evidences of irregularity in size and discontinuity in development and differentiation are not, in my opinion, the more serious of the objections raised. Such differences may indeed be explained as cœnogenetic. Rabl himself has given the evidence ('89) that the first rudimentary visceral cleft is differentiated later than the second. Moreover, it is well known that the first rudimentary myotome in *Amphioxus* develops later than the following. Differences in time of development and of differentiation are to be expected when a comparison is made between the Anlagen of serial organs, some of which become highly differentiated (e. g. the eye muscle somites, 1st, 2d, and 3d), while the others (e. g. the anterior, the 4th, and the 5th somites) are becoming rudimentary. It is interesting to find that the last intersomitic constrictions to be formed are those between the anterior and the 1st cavity, and between somites 4 and 5, that is, the constrictions separating the most rudimentary somites. The separation of the anterior somite from the premandibular is first complete in an embryo with 26 or 27 somites, while the constriction between somites 4 and 5 appears first in an embryo with 28 somites. Consequently van Wijhe's statement, that the segmentation of the dorsal mesoderm begins in the neck region and proceeds continuously anteriorly and posteriorly, is true only in part. But it also follows that the discontinuity in the development of the more anterior constrictions may be explained as in great measure due to degeneration. The retardation in development due to degeneration, already apparent in the 1st somite of *Amphioxus*, makes itself manifest in the somites of the more highly specialized *Squalus* as far posteriorly as the 7th somite of van Wijhe (equivalent to the 8th somite of *Amphioxus* ?), which I believe to be *the first somite differentiated, as well as the first to develop a permanent myotome*.¹ The correlation between degeneration and retarded development serves to explain, for the occipital somites at least, why the development of the somites in the Craniota begins in the neck

trunk. Such purely topographic relations in the Selachian cannot be regarded as weighty evidence in the settlement of this question, in comparison with the evidence stated for *Amphioxus* (van Wijhe, '93, Hatschek, '92), *Bdellostoma* (Price, '96*), and *Amphibia* (Houssay, '91, Platt, '94), which has led these investigators to regard the visceral clefts as intersomitic in position. In view of the great probability of a shoving forward of the visceral clefts with reference to the somites in *Squalus*, I am unable to accept Hoffmann's conclusion on the basis of the evidence he presents.

¹ On account of the considerable variation in the length of embryos in early stages of development, I am unable to state positively that the seventh somite is the first to develop. It may be the eighth somite which does so, as stated by Hoffmann ('94, '96). The seventh somite shows some signs of degeneration, having a small myotome and losing its ventral nerve during development.

region. So far as I know, hitherto no explanation of this phenomenon has been suggested.

That which I have regarded as the more serious of the objections made by Rabl ('89 and '92), viz. that the pre-otic segments are not morphologically comparable with trunk somites, inasmuch as they do not show a differentiation into myotome and sclerotome, may be met by a denial of the statement, so far as it applies to the 3d somite of van Wijhe.¹ I have followed the development of this somite through closely connected stages of development, until it becomes converted into the musc. rectus posterior and assumes relation with the eye, in order to determine

whether in its development it exhibits those marked differences which, as stated by Rabl, serve to distinguish pre-otic and post-otic mesodermal segments. The evidence which I have obtained may be summarized as follows: Cross sections of embryos in early stages of development leave no doubt that the 3d somite, as its topographical relations to chorda, dorsal aorta, epibranchial line, and dorsal wall of alimentary canal show, is composed of only dorsal mesoderm. Figure A represents a cross section in the region of this somite from an embryo with 28

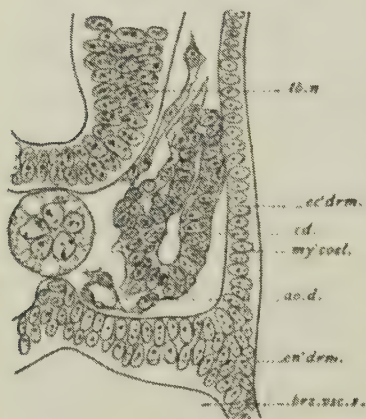


FIGURE A.

somites (compare Plate 3, Fig. 13). It is seen that a well marked cavity (myocoel), surrounded by a single layer of epithelial cells, may be distinguished.²

¹ Both van Wijhe ('82) and Killian ('91) have affirmed a differentiation of head segments into myotome and sclerotome.

² That the epithelial walls of the cavity (Fig. A) are not continuous with the two layers of the lateral plates is due to the obliteration of these two layers caused by the great development of the first visceral pouch.

Fig. A. Cross section of a *Squalus* embryo in the region of van Wijhe's 3d somite and encephalomere IV. $\times 240$. The dorsal nature of this mesodermal segment is attested by its relations to dorsal aorta and wall of alimentary tract. At this stage (Acraniens stadium) the region of proliferation of mesenchyma is seen to be a definite one, and to correspond in its relations with the sclerotome of trunk somites.

ao. d., dorsal aorta; brs. vsc. I, first visceral pouch; cd., chorda dorsalis; ec'drm., ectoderm; en'drm., entoderm; my'coel., myocoel, enlarged ventrally to form a sclerotome vesicle; tb. n., neural tube.

The cavity of the somite is enlarged ventrally opposite that portion of its median surface where a rapid proliferation and migration of cells appears to take place. I see no reason why the more dorsal and lateral portion of the mesoderm should not be homologized with the myotome portion, and the ventral median region with the sclerotome portion of trunk somites. I am unable to detect any essential difference between the phenomena presented in this section and those presented in sections made in the region of van Wijhe's 5th and 6th somites, to which Rabl grants "Bürgerrecht" as true somites. The greater dorsal extent of the latter cannot be regarded as an essential difference. Here, as there, we find a well marked and definite region of cell proliferation. As development goes on, the cavity of the 3d somite increases in volume, and at the same time the somite grows forward, chiefly by the elongation of its anterior end, median to the Gasserian ganglion. In confirmation of the statement of Miss Platt ('91), I find that the first muscle cells are differentiated in the median wall of that portion of the somite which at this stage lies posterior to the Gasserian ganglion. The great extension of the anterior portion seems to retard its histological differentiation. But in this portion also, when muscle cells appear, they are found in the median wall. Rabl ('89, p. 236) says: "Während ferner die Muskulatur der Urwirbel ausschliesslich aus der medialen Wand ent-

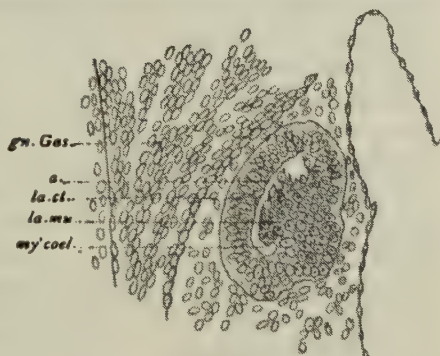


FIGURE B.

steht, nimmt sie im Vorderkopf zum grössten Theil aus der lateralen und zum kleineren Theil aus der hinteren Wand der sogenannten Somite den Ursprung." A cross section of the myotome of the 3d somite at a late stage of development appears to me to refute this statement (Figure B). It is clear from an examination of the phenomena presented in such a

FIG. B. Portion of a cross section through the middle of the myotome of van Wijhe's 3d somite, in a late stage of development (20 mm.). Elongated muscle cells are already differentiated in the median wall (muscle plate), while the lateral wall (cutis plate) retains its epithelial character. $\times 50$.

a, cell migrating from the median wall of the myotome into the myocoel; gn. Gas., Gasserian ganglion; la. ct., cutis plate; la. mu., muscle plate; my'coel., myocoel.

section, that the greater part of the cells proliferated into the cavity of the myotome, the cells of which are at this stage already converted into elongated muscle cells, arise from its median wall. While the outer wall still maintains its primitive epithelial character, the inner wall has become many cells in thickness and some of these cells appear in the act of migrating into the now greatly diminished lumen of the cavity. Later, however, the cells of the outer wall also are converted into muscle cells, and thus both walls of the cavity participate in the formation of the *musculus rectus posterior*. We have therefore in the 3d somite of van Wijhe a pre-otic segment of the dorsal mesoderm, which becomes differentiated into myotome and sclerotome, and whose musculature is derived in greater part from its median wall. Furthermore, as is well known, its musculature is innervated by a nerve (*abducens*) which all the later morphologists, with, so far as I know, one exception (Kupffer, '94, '95), regard as a ventral nerve comparable with spinal ventral nerves. Finding this to be the case with at least one pre-otic mesoderm segment, we are in a better position than we otherwise should be to understand the more modified, or at least more divergent, conditions presented by the remaining pre-otic segments, viz. the anterior, the 1st, the 2d, and the 4th. That in these segments marked peculiarities appear is certain. In the 4th somite we have a segment of the dorsal mesoderm divided by constrictions from the 3d and 5th somites at a time when it presents essentially the same evidences of differentiation into myotome and sclerotome which appear in the 3d and 5th somites. That no muscle cells are formed in its inner wall, and that it soon breaks up into loose mesenchyma, are phenomena which are to be expected in a somite destined to become rudimentary. That it is more rudimentary than the 5th somite is due to the development of the otic capsule, under which it lies. The 5th somite — in whose inner wall elongated cells appear, without however developing into muscle fibres (as stated by Sedgwick, '92) — thus forms a natural transition to the conditions presented by the 4th. If the 3d and 5th are to rank as somites, it is in my opinion impossible to deny that the 4th, which lies between them, is serially homologous with them, even though it should lack some of the characteristics of a typical trunk somite.

Passing forward in the embryo to the 2d (mandibular) somite, it seems to me indisputable that this is the anterior continuation of the dorsal mesoderm. In very early stages it grows ventrally to form the mesoderm (mesothelium) of the mandibular arch, a process which, according to Kupffer ('88), occurs in *Petromyzon* also. However, only the dorsal part of the "mandibular cavity," which later becomes separated

from the ventral to form the musc. obliquus superior, can by virtue of its topographic relations to chorda and aorta be regarded as the somatic portion of this mesoderm segment (Plate 7, Fig. 56). Its ventral portion, which later becomes differentiated into the musc. adductor mandibulae, is therefore splanchnic. While the indications of the differentiation of the 2d somite into myotome and sclerotome are less clearly expressed than in the case of the 3d and 4th, I have no reason to question the correctness of Killian's ('91) interpretation that such appear. The great enlargement of the cavity of the somite is the chief factor in modifying its form and the relations of its constituent parts. While Miss Platt ('91) finds the musculature to arise first in the median wall of the somite, that is to say, the *dorsal* part of the so called "mandibular cavity," Hoffmann ('96) states that the musc. obliquus superior arises in its upper and lateral walls. In my opinion their conclusions are not so divergent as they might at first sight seem to be, for I believe that the portion of the somite which Hoffmann calls dorsal is morphologically *median*; in other words, that it is the portion which in early stages lies against the wall of the neural tube (Plate 7, Fig. 56). I agree with Hoffmann that the musc. obliquus superior arises in the dorsal and lateral walls of the second (van Wijhe's) somite, but with the qualification that the dorsal wall is morphologically median.¹

The first (premandibular) somite shows in its development even greater peculiarities than those of the mandibular; yet it appears to me to possess somatic value as unquestionably as the latter does. The first and most important question to answer is whether this segment represents dorsal mesoderm or a diverticulum from the alimentary canal, and for this purpose the relations of the connecting stalk furnish us with the decisive evidence. In a median sagittal section of an embryo with 14 or 15 somites, such as that shown in Figure C, the tissue which is later differentiated as the connecting stalk of the first somite appears as a mass of cells between the base of the brain, in that region which lies just posterior to the pit of the infundibulum, and the dorsal wall of the alimentary canal. Posteriorly this mass of cells is continued into the chorda and its relations are seen to be such that, if the chorda is dorsal, so must the mass of cells be also. The lumen of the alimentary canal may be traced to a point directly ventral to the pit of the infundibulum, where it ends as the so called "Seessel'sche Tasche" (Kupffer's "prä-

¹ Miss Platt's ('91) evidence of the continuity of the cavity of the alimentary canal and that of the mandibular cavity, as well as her evidence of two segments in the latter, appears to me illusory.

orale Darm"), while its walls become continuous anteriorly with that mass of tissue which later differentiates into the "anterior cavities." Furthermore, a cross section of a corresponding stage of development in a plane immediately posterior to the infundibulum (i. e. along the line $\alpha\beta$ of Figure C) gives equally convincing evidence (shown in Figure D) that the mass of cells (1) lies *dorsal* to the wall of the alimentary canal, with which, however, they are in close connection in this somewhat earlier stage (11-12 somites). There exists not the faintest shadow of evidence that the mass of cells which forms in its lateral part the premandibular cavities and in its median part their connecting stalk, represents entoder-

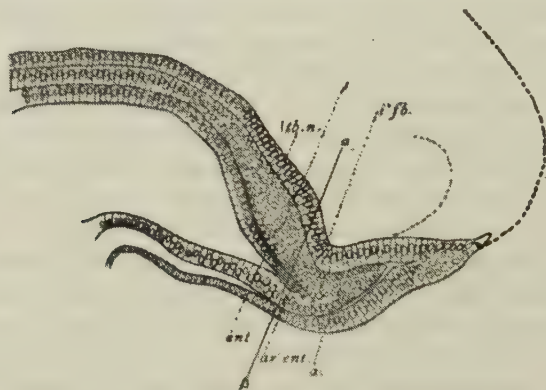


FIGURE C.

mal diverticula. During development, as the result of the ventral growth of the infundibulum, the pre-oral (Seessel's) pouch becomes obliterated and the mass of cells surrounding the "anterior cavity" is cut off from those posterior to the infundibulum (26-27 somites). By this change in relations the Anlagen of the connecting stalk and of the premandibular cavity take a position apparently *anterior* to the alimentary canal and in close

FIG. C. Median sagittal section of a *Squalus* embryo with 14 or 15 somites. The neural folds have not as yet met in the mid-dorsal line. $\times 77$. The mesoderm of the connecting stalk of van Wijhe's first somite is seen as a thickened mass of cells lying between the base of the brain and the dorsal wall of the alimentary tract.

1, mesoderm which later becomes differentiated as the connecting stalk of the first head cavity. α , mesoderm of the "anterior cavity" (Platt); $ar'ent.$, pre-oral pouch of the archenteron; $ent.$, dorsal wall of alimentary canal; $i'fb.$, infundibulum; $tb. n.$, ventral wall of the neural tube; $\alpha\beta$, projection of plane of the section shown in Figure D.

connection with the ectoderm immediately posterior to the infundibulum. Still later (40 somites) cavities appear both in the median connecting stalk and in the lateral mesoderm; and these by their fusion form the continuous cavity in the manner already described by Miss Platt ('91^a). It follows therefore that the premandibular cavities comprise dorsal and only dorsal mesoderm,¹



FIGURE D.

¹ Hoffmann ('94, p. 648), however, finds evidence of a splanchnic portion of the premandibular somite in a "Zellstrang, welcher dem Mandibularbogen parallel verläuft und der Vorderfläche dieses Bogens unmittelbar aufliegt" (his Fig. 4 x, p. 648). He adds, "Ein Lumen dieses Bogens habe ich in diesem Strange nie gesehen," and he uses this evidence to support his conclusion that the mandibular arch is double. I can confirm Hoffmann's statement as to the presence of this "Zellstrang" in the anterior portion of the mandibular arch; but there is another cord, not mentioned by Hoffmann, which is in every respect similar to this one and extends parallel and close to the posterior wall of the arch. I hold Hoffmann's interpretation, however, to be incorrect, since, according to my determination, the cells of these strands are in large part if not entirely ectodermal in origin, i. e. derivatives of the neural crest. The cells of the Anlage of the Trigemini may be followed in closely connected stages as they migrate ventrad until they enter the mandibular arch, where they come to surround the mesothelium as a ring of loose cells between the mesothelium and the superficial ectoderm. This evidence confirms the previous results of Kaatschenko, Platt, and Goronowitsch ('93). While the fate of these cells is not clear to me, Miss Platt ('94 and '97) finds that in *Necturus* they contribute in large part to the formation of the cartilage of the mandibular arch. Considering the similarity in the origin of the anterior and posterior cell strands, as seen in parasagittal sections through the mandibular arch, it becomes noteworthy that Hoffmann ('94) in his preliminary paper failed entirely to reproduce in his figures the posterior, while in his later paper ('96, Taf. III. Fig. 22), he figures two cell strands as histologically quite different from each other. This appears to me a notable illustration of the prejudicial influence of a theory. Although I

FIG. D. Cross section of a *Squalus* embryo with 11 or 12 somites in a plane corresponding with that of the line $\alpha\beta$ of Fig. C. $\times 50$. The section shows clearly the dorsal position of the connecting stalk of van Wijhe's first somite (I) in relation to the pre-oral pouch (ar'ent.).

I, mesoderm of the connecting stalk of van Wijhe's first somite; ar'ent., archenteron = pre-oral pouch; cl. crs. n., neural-crest cells; ec'drm., ectoderm; ent., mesoderm; i'fb., infundibulum; tb. n., neural tube.

and it may also be inferred that the median portion of the connecting stalk is morphologically the undifferentiated anterior portion of the chorda, while the more lateral portions of the connecting stalk may be regarded, as they have been by Killian ('91, p. 102), as representing the sclerotome of the somite. Furthermore, the inference drawn by Froriep ('92*), on the ground of evidence presented by Kastschenko ('88) and Kupffer ('88, '90, '94), that the lumen of the connecting stalk must be ventral and morphologically a part of the procoelom, receives no support. If Kupffer's statement that the premandibular cavities of *Ammocoetes* are formed as diverticula from the alimentary canal is correct, their development in *Ammocoetes* must differ essentially from that in *Squalus*. Goette ('90), however, flatly contradicts Kupffer's statements. My own observations on *Ammocoetes* lead me unhesitatingly to accept the evidence presented by Goette.¹ Besides, the criteria furnished by the study of the early stages of development of the premandibular cavity in *Squalus* seem to me more satisfactory, because more decisive, than the evidence used by Kupffer ('93*, p. 522) to demonstrate the ventral nature of the connecting stalk of the premandibular cavities in *Ammocoetes*, viz. the relation to a blood-vessel which is only hypothetically the complete homologue of the dorsal aorta. I find this blood-vessel in embryos of *Ammocoetes* of somewhat advanced stages of development (4 mm.) extending above the connecting stalk of the premandibular cavities, as the apparent anterior continuation of the dorsal aorta, as stated by Kupffer. But there is also ventral to the connecting stalk a similar blood-vessel, which unites with the dorsal vessel both anterior and posterior to the connecting stalk. It is consequently difficult for me to comprehend why the more dorsal vessel rather than the more ventral one is to be regarded as the anterior continuation of the dorsal aorta. Kupffer gives no reasons, simply stating that the ventral vessel can be homologized, if at all, with the carotis ventralis of *Mammalia*. Now, if we are to apply rigidly such a criterion as Kupffer's to

am unable to accept Hoffmann's conclusion on the basis of the evidence he presents, I believe there are good grounds for holding that a visceral arch, which once existed between the mandibular and the hyoid (first and second visceral) arches, has disappeared in phylogeny. The evidence in favor of this view will be summarized later.

¹ That Kupffer has not in his studies come to a right understanding of the development of the anterior head mesoderm seems to me certain from a comparison of my sections with those figured by him ('90, Figg. 31 und 32, Taf. 28). The cells which he calls ganglionic are in my opinion the anterior mesoderm. This appears to me to be Kupffer's fundamental error.

determine what is dorsal and what is ventral, it would follow from the evidence already stated by Platt ('91) that the anterior portion of the dorsal aorta in *Squalus* embryos comes to lie in part *dorsal* to the chorda, and therefore that this organ, commonly known as chorda *dorsalis*, could more correctly be named chorda *ventralis*. Kupffer's argument thus leads to a *reductio ad absurdum*.

According to Hoffmann ('96) the muscles innervated by the oculomotorius have their origin from the posterior part ("Fortsatz") of the premandibular cavity. Because of the complicated development and the secondary subdivisions of this cavity, it is difficult to be certain; yet it seems to me that, as in the case of the second and third cavities, the epithelium of both median and lateral walls participates in the production of the muscles formed from this cavity, viz. musc. obliquus inferior, and recti inferior, superior, and anterior.

Before passing to a consideration of the nature of the "anterior cavities," I wish to discuss, in connection with the preceding study of the morphology of the eye-muscle somites in *Squalus*, the evidence of the development of the eye muscles of *Petromyzon* which has been given by Hatschek ('92) and Kupffer ('94), and to determine in how far this brings us to an understanding of the morphology of the eye muscles in Vertebrates in general. The repeated confirmation of Marshall's conclusion that the eye muscles in *Selachii* and *Reptilia* are derived from the epithelium of the first, second, and third cavities—van Wijhe ('82), Dohrn ('85), Orr ('87), Kastachenko ('88), Miss Platt ('91), Oppel ('92), Hoffmann ('96), and myself—seems sufficient to remove any doubt (so far as those groups of animals are concerned) which Kupffer ('94) may have sought to throw upon that conclusion. In Amphibia, Birds, and Mammals, as is well known, the eye muscles are differentiated from the connective-tissue capsule surrounding the eye. Although the source of these cells is not known with certainty, there is no reason to doubt that, as in *Selachii* and *Reptilia*, they have their origin from the dorsal mesoderm. In direct contradiction to these facts, which hold true for higher Vertebrates, stand the conclusions of Hatschek and Kupffer, that in Cyclostomes the eye muscles are splanchnic in their origin, i. e. derived from the mesoderm of the visceral arches. Let us examine the evidence given by them, in order to determine in how far it seems to warrant their conclusions. Hatschek's briefly summarized evidence has been stated on pages 192, 193, and needs no repetition.

In sections of a 5 cm. *Ammocetes* I find the relationship of the median posterior musculature of the eye capsule to the velar muscle,

which is the probable homologue of the *musculus adductor mandibulae* of *Selachii*, to be those stated by Hatschek. Whether in this muscle group we have to do with the *musculus obliquus superior*, I am not able to state, since its innervation still remains uncertain to me.¹ I know, however, that it is not innervated by the *oculomotorius*. Its fibres, moreover, are not continuous with those of the velar muscle at this stage of development, if indeed they are at any stage. Hatschek's chief evidence that this muscle is derived from the velar muscle apparently consists in their histological resemblance, which he states is complete. At the stage studied by me this is certainly untrue. For I find that while the velar muscle is composed of large fibres, at least 7μ in diameter, the fibres of the muscle in question are in their widest part not over 3μ in diameter, and also that, while the fibres of the former show well marked longitudinal and cross striations, those of the latter show these very faintly. Moreover, the nuclei of the former are for the most part round or oval, while those of the latter are exceedingly elongated. It is of course possible that Hatschek bases his statements on the examination of the histological conditions in embryos of a different stage of development. But even if we grant that the *musculus obliquus superior* in *Cyclostomes* is, as in the *Selachii*, derived from the dorsal part of the musculature of the mandibular arch, this evidence no more warrants the conclusion that the muscle is splanchnic in origin in the former group than in the latter. Of its dorsal origin and somatic nature in the latter group, proof has been given above.

Even more theoretical than his conclusions concerning the origin of the *musculus obliquus superior* appears Hatschek's inference that the eye muscles innervated by the *oculomotorius* are derived from the constrictors of the visceral arches, a conclusion which he draws apparently by the method of exclusion. It does not seem to have occurred to him that these muscles may have had their origin from the connective-tissue capsule of the eye, the cells of which are in my opinion derived from the dorsal mesoderm in this region, which in early stages becomes disintegrated and surrounds the eye vesicle. Kupffer ('94) thinks that the more difficult part of the task of tracing the development of the eye musculature in *Ammocetes* is accomplished when he has followed the growth of muscle cells from the so called "Trabekular" and the mandibular arches until they come into close relation with the eye capsule in

¹ That Hatschek ('92) incorrectly identified the *musculus rectus posterior*, has been shown by M. Fürbringer ('97) from the study of its innervation, a matter to which Hatschek seems to have paid no attention.

a 6 mm. embryo. In consideration of the facts that he does not even know that these muscle cells become differentiated into the eye muscles, and that he has not determined their innervation, the doubt which he seeks to throw upon the results which differ from his own appears quite unwarranted. Furthermore, I find that the anterior and posterior velar muscle strands described by Kupffer are in essentially the same relations to the eye capsule in stages of 6-9 mm. as in those of 5 cm., and that these strands show no relation — except that relation of the posterior (mandibular) muscle strand described by Hatschek ('92) — to the eye muscles, which are already clearly differentiated in the latter stage. I must therefore conclude that Kupffer has not seen the early stages of the development of the eye muscles of *Ammocetes*. I regard the determination of their origin in this animal as an embryological task yet to be accomplished, — a task in which the well known difficulty of obtaining material in stages between 9 mm. and 30 mm. will be encountered. For it is in these stages, in my opinion, that the eye muscles are differentiated.

I turn now to the development of the "anterior cavity," which has been so thoroughly studied by Miss Platt ('91, '91*) and by Hoffmann ('96) that I need say but little, and that of a general nature. It seems very clear, since the "anterior" mesoderm segment develops from a perfectly solid mass of cells anterior and lateral to the infundibulum of the brain, that the statement of their formation as lateral diverticula of the alimentary canal is purely hypothetical. It seems also warrantable to infer that the connecting stalk which unites the lateral halves of the segments in early stages of development, the cells of which according to Hoffmann ('96) entirely disappear, represents in part the anterior continuation of the alimentary canal. But it is impossible to state, because of want of such criteria as chorda and dorsal aorta, whether we have here to do with dorsal mesoderm. Without proof to the contrary, and with the evidence that these cavities assume a histological appearance similar to that of the following ones, I conclude with Platt and Hoffmann that the "anterior" mesoderm segment, which appears, so far as is known, in only two *Selachii* (*Squalus* and *Galeus*), is serially homologous with those behind it. I am able to confirm the evidence given by these two observers, that mesenchyma cells migrate into the lumen of the cavity in the later stages of its development, and to confirm the former, that such cells first migrate from the median wall (Figure E), in which also some cells assume an elongated spindle form, possibly indicating rudimentary muscle cells. Such histological evi-

dence would seem to tell in favor of the view that this mesoderm segment, like the following ones, is to be regarded as of somatic value.¹

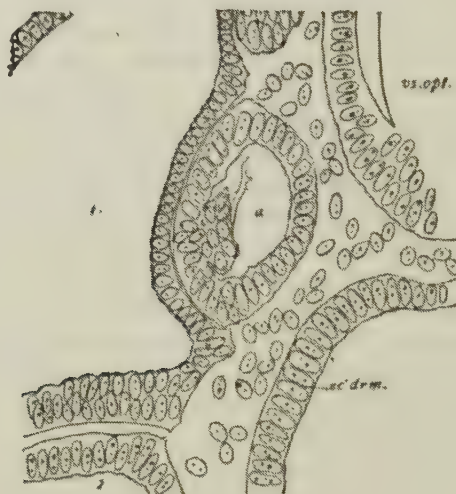


FIGURE E.

d. SUMMARY.

Neuromeres and somites show an exact numerical correspondence throughout the length of the embryo. The serial alternation of myelomeres and somites evinces the metamerism of the former, while the exact numerical correspondence of the encephalomeres and head somites appears equally convincing evidence of the metameric value of the encephalomeres. The head somites in *Squalus* are homologous with those described by van Wijbe ('82) for *Scyllium* and *Pristiurus*, and there is yet another anterior to these, viz. the "anterior" somite first

¹ As the most anterior of the cavities of the Selachian embryo, it would seem more probable that the anterior cavities described by Miss Platt should be homologized with the "head cavities" (vordere Entodermtasche) of *Amphioxus*, than that the next following, the premandibular, should be.

FIG. E. A cross section through the "anterior cavity" (frontal section of the embryo) in an embryo with 78 somites. $\times 240$. To show the proliferation of cells into the myocoel from the median wall of the cavity.

1, 2, first and second head cavities; a, "anterior cavity" (Platt); ec'drm., ectoderm; vs. opt., optic vesicle.

seen by van Wijhe in Galeus. The somatic value of the post-otic head somites is indisputable. The pre-otic somites, five in all, are also in my opinion homodynamous with trunk somites. They are segments of the dorsal mesoderm (with the possible exception of the "anterior"), which, as exemplified in the third somite (van Wijhe's), become differentiated into myotome and sclerotome. While the "anterior" and the fourth somites become rudimentary and develop no muscle fibres, the eye muscles are differentiated from the median and lateral walls of the first, second, and third. The eye muscles of Selachii are therefore somatic in their origin, not splanchnic,¹ as has been held by Hatschek ('92) and Kupffer ('94). It will furthermore be shown that the nerves which supply them are serially homologous with ventral spinal nerves. It is to the consideration of the nerve relations that I now pass.

VI. The Relation of Neuromeres to Nerves.

Ahlborn ('84*) said: "Es bleibt auch im Auge zu behalten, dass die gesammte Neuromerie secundärer Natur ist: sie ist nur eine Wiederbohlung aller vor ihr entstandenen Metamerien des Körpers. Eine primäre Metamerie, wie sie z. B. im dorsalen Mesoderm vorliegt, ist weder im centralen, noch im periferischen Nerven-system vorhanden,² und wenn im Rumpfe die Neuromerie mit der primären Mesomerie übereinstimmt, so reicht diese Eigenschaft im Allgemeinen nur so weit, als die Nerven sich innerhalb des primär segmentirten Mesoderms befinden, und sie hört auf, wenn die Nerven in solche Organe eintreten, die ausserhalb der Mesomeren liegen, oder die in einer anderen nicht segmentalen Metamerie entwickelt sind."

In the trunk, the arrangement both of myelomeres and nerves is clearly metameric, being correlated with the segmentation of the mesoderm. Related to each mesodermal somite is a ventral nerve (motor root), which arises from segmentally arranged groups of ganglionic cells in the anterior (ventral) horn of the spinal cord, that is, from each myelomere. Into the posterior (dorsal) horn pass the fibres of the dorsal nerve, which have their peripheral distribution in the skin of that segment (rami cutanei) and in the intestine (sensor and motor sympathetic fibres).

In a study of the simple, and it has been assumed primitive relations in the trunk, it is important to consider not only the peripheral distribu-

¹ With the exception of the musc. rectus posterior (Hatschek).

² Compare Froriep ('94).

tion of nerve fibres, but also their distribution in the central nervous system. Gaskell ('89) has rightly insisted that the position of the cell groups which are in connection with the nerve fibres, is the true criterion of what forms a nervous metamere, rather than the position of the exits of the nerve fibres. The shifting of nerve roots is too well known to need discussion here. In regard to sensor nerves Miss Platt ('96) says: "Both development and comparative anatomy tend to show that it is a matter of little moment whether these fibres [of the lateral-line nerves] enter the brain by one nerve root or another." I find as a result of my own studies that the ganglionic cells of cranial nerves enter into fibrillar relation with the neural tube at points quite widely separated from the encephalomere from which the cells were proliferated, and also that in embryos of different Vertebrates the relations of the fibres of the same nerves to the encephalomeres are variable, not only in the case of ganglionic roots but of medullary roots also, as those of the trigeminus, abducens, and glossopharyngeus. In the swine and the chick the abducens arises from encephalomere VI, whereas in *S. acanthias* it is in relation with encephalomere VII. Also in swine and chick the root of the glossopharyngeus is in relation with encephalomere VII, whereas in *S. acanthias* it passes from the neural tube posterior to this neuromere. It is obvious, then, that we must take into consideration, particularly in the case of cranial nerves, both the location of the "Kerne" of the medullary roots, and the points or regions of proliferation of the ganglionic cells of ganglionic roots, in order to determine their primitive relationships.

a. HISTORICAL REVIEW.

An examination of the literature bearing on the question of the relation of nerves to neuromeres is rendered difficult by the fact that many investigators have failed to distinguish between medullary and ganglionic nerve relations, and thus have not made clear what they meant by the statement that a nerve "develops" from, or has its "origin" from, the expansion or constriction of a neuromere. The figures of McClure ('90) and of Waters ('92), for example, show a proliferation of the ganglionic Anlagen of nerves from the neuromeres, but not the relationship of the neuromeres to *nerve fibres*. While it seems very probable that the proliferation of ganglionic Anlagen has a bearing on the primitive relationship of the dorsal nerves (sensor portion), our best criteria of the segmental value of encephalomeres, as well as of myelomeres, is their relation to medullary nerves, — i. e. ventral nerves

and the motor components of the dorsal nerves. Furthermore, we must determine the primitive relations of medullary nerves, not by the place of exit of their fibres (i. e. by their roots), for we know these to be variable, but by the position of their "Kerne" in the walls of the neural tube.¹

There is considerable difference of opinion as to whether nerves ("roots") arise primarily from the expanded portion of the encephalomere (or myelomere), or from the constrictions between these segments. As early as 1878 Marshall said, "My investigations tend very strongly to prove that all the nerves arise primitively from the widest parts of the dilated vesicles, whether of brain or cord, and never from the intervening constrictions." Later, McClure ('89), who is in agreement with Marshall as well as with Orr, Béraneck, and Waters, said, "The dorsal roots of spinal nerves take their origin from the apex of their respective myelomeres in exactly the same manner as the nerves of the medulla do from their respective encephalomeres." Minot ('92) criticises McClure for overlooking the fact that the "neuromeres can have no genetic relation to the ganglionic nerves." The ground of Minot's statement does not seem to me to be so self-evident as not to be in need of explanation.²

In disagreement with McClure, Miss Platt ('89) claimed that "the concavity in both medulla and spinal cord is the source from which the nerve originates," and her conclusion, which Minot accepts, is that the origin from the expanded portion of the neuromere is secondary. In view of this difference of opinion it is of interest that Balfour ('85) stated that in Selachian embryos the dorsal and ventral roots of spinal nerves alternate with each other, the dorsal roots being intersegmental (intersomitic) and the ventral roots segmental (somitic) in position. Miss Platt did not, however, in her statement of nerve relations make a distinction between dorsal and ventral nerves.

¹ The most serious obstacle to the use of this criterion is the difficulty of applying it in those early stages of development when metameric relationships appear least modified. Martin ('90 and '91, p. 230) has noted an ontogenetic ventral shifting of motor "Kerne" in the cat.

² It is to be regretted that McClure gave no figures of the nerve relations of myelomeres. Minot apparently assumes that the neuromeres are constituted solely in adaptation to a motor segmentation, and therefore that the neuromeres are segmental localizations of ganglionic cells (i. e. motor "Kerne") in the wall of the neural tube, just as are the segmental ganglia of Annelida. It seems to me therefore that McClure might have met Minot's criticism by reminding him that neurologists have recognized in the medulla groupings of ganglion cells which are in relation with sensory fibres, i. e. sensory "Kerne" or "Endkerne" (see Edinger, '96, p. 866), and may well contribute to the metameric enlargements.

b. NERVE RELATIONS IN THE TRUNK OF *S. ACANTHIAS*.

An examination of sections in the trunk region of embryos of *S. acanthias* leaves no doubt whatever that the chief proliferation of ganglionic cells occurs in the regions of constriction between myelomeres, i. e. opposite the somites, and that the ventral roots also arise opposite the somites. Motor roots appear long before the sensor roots, as was first stated by Sagemehl ('82). Dohrn has affirmed that they arise as early as Balfour's stage H. I find them in embryos of *S. acanthias* in which 34 somites are differentiated, stage H. From the very first, i. e. at this early stage, they are in relation with the ventral portion of the neural tube at a point directly opposite the middle of the somite. That the relation with the tube is opposite the *middle of the somite* is most easily demonstrated in frontal sections (see Plate 6, Fig. 42, which represents a frontal section of an embryo with 50 somites); but that their relation is with the *ventral* wall of the tube, is most clearly seen in cross sections (Plate 6, Fig. 41, *rx. v.*). In frontal sections more dorsally situated than those which show the ventral roots, the spinal ganglia are likewise seen to lie opposite the middle of the somites¹ (Plate 6, Fig. 43). In later stages, however, the spinal ganglia lie opposite the anterior portion of the somites, i. e. intersomitic in position, as a result, probably, of the shifting of the somites. Since by this time the constrictions between myelomeres have disappeared, *it is quite impossible to state that dorsal roots arise either from the constrictions or from the dilatations of the myelomeres.*

McClure ('90, p. 42) has said that in the forms studied by him "the dorsal branches of the spinal nerves pass from the external surface of the myelomeres to the space between two somites, which is opposite their point of origin, and fuse with the epiblastic thickenings to form the spinal ganglia." Such a statement, if true, is certainly of great importance in settling the question of the morphology of cranial nerves. For it is now generally stated by morphologists that the chief distinction between spinal and cranial nerves consists in the fact that the ganglia of cranial nerves receive cellular material during development from the ectoderm of the lateral surface of the head, whereas the spinal ganglia do not. So far as I know, McClure's statement remains unconfirmed,

¹ Similar relations of dorsal ganglia and ventral roots have been shown by Marshall ('78, Plate III. Figs. 27 and 28) for birds; by Hoffmann ('90, Taf. CLV. Fig. 7) for reptiles; by Dohrn ('91, Taf. V. Figg. 16 und 17) for Selachii; and by Sewertzoff ('95, Taf. V. Fig. 16) for Amphibia.

and it is certainly not true for *Squalus*, and not true, so far as I am able to determine, for *Amblystoma*. In *Petromyzon*, however, as has been previously stated by Scott ('87) and Shipley ('87), the spinal ganglia lie opposite the constrictions between the somites (in later stages opposite the myosepta).¹ Thus, inasmuch as the dorsal nerves of *Ammocetes* are *intersomitic* and never unite with the ventral nerves which are *somitic* in position, and inasmuch as the dorsal ganglia show close connection with the ectoderm in early stages of development and lose this connection during development, the spinal nerves of this animal form a natural transition from the nerves of *Amphioxus* to those of *Squalus* and higher Vertebrates. For in *Amphioxus* ventral nerves are somitic in position, dorsal nerves intersomitic, and the connection of the ganglia of the latter with the skin is retained throughout life.² Two chief causes seem to have brought about the change in the relations of the dorsal spinal nerves in the Vertebrate series. The first cause appears to have been the great dorsal and anterior extension of the trunk myotomes, and the second cause the posterior extension of the ramus cutaneus dorsalis vagi (ramus lateralis vagi), which takes the place of the rami cutanei of the spinal nerves. The physiological reason for the extension of the vagus is to be found in the advantage obtained from the centralization of sensory impulses in the brain. With van Wijhe ('92), Hatschek ('93), and M. Fürbringer ('97), I accept the theory of Prochaska, Sömmering, and Gegenbaur that cranial and spinal nerves are homodynamic, and the view of Hatschek ('92) that dorsal and ventral nerves primitively alternated with each other.³ Of these, the former were mixed in function and the latter motor, as in *Amphioxus*.

c. NERVE RELATIONS IN THE CEPHALIC REGION OF *S. ACANTHIAS*.

In the head, where the nerve relations are much more complicated, it will be necessary to trace the development of the nerves in different stages. The series represented in Figures 7 to 21 (Plates 3 and 4) is intended to show the changes which the neural crest (colored in blue) undergoes, and likewise to show the development of the brain vesicles

¹ Because of this relation to the myomeric constrictions in *Ammocetes* and the relation of the ganglia to the *expansions* of the spinal cord (myelomeres) deducible from it, it is obvious that not very great morphological value can be given to the fact that in *Squalus* the ganglia lie opposite the *constrictions* of the spinal cords.

² I hold with Hatschek ('92) and M. Fürbringer ('97) that in *Amphioxus* the homologues of the dorsal ganglia of *Craniota* are found in the cell groups at the place where the dorsal nerves meet the skin.

³ See also Ransom and Thompson ('86).

up to the time when a fibrillar connection of the nerves with the neural tube is effected and the chief peripheral branches are differentiated.¹

Minot ('92) and Mitrophanow ('93) have stated that the neural crest in Selachii is not differentiated before the closure of the neural tube, and Rabl ('89) found that in *Pristiurus* embryos the "Trigeminus Anlage" first appears at a stage with 18 somites. On the other hand, Beard ('88) and Dohrn ('90) have shown that in some Selachii,² as well as in Sauropsida, the neural crest is differentiated in the region of the head before the closure of the neural tube.

As has been previously stated, my observations confirm those of Beard and Dohrn, since I find that at an early stage, when the cephalic plate is still widely open, the fundament of the trigeminus is clearly differentiated from that portion of the neural plate which is destined to form the neural tube. The disassociation of the neural-crest cells in this region and their resultant loss of compact arrangement have taken place to a considerable extent before the neural folds meet in the mid-dorsal line. Usually the neural folds first close in the trunk region behind the cephalic plate, and later in the region of the midbrain, i. e. in the region of the "Trigeminus Anlage." The closure of the cephalic plate occurs last in the forebrain, where the "neuropore" persists for a considerable period.

At a stage with 15 or 16 somites (Plate 3, Fig. 7), when the cephalic plate is closed except in the region of the forebrain, the neural crest is clearly differentiated in that region of the brain which extends from the constriction between forebrain and midbrain to the anterior constriction of hindbrain neuromere (encephalomere) IV, i. e. in the region of the so called cephalic flexure. In the region of encephalomere IV a few cells with protoplasmic processes occur in the space between the neural tube and the overlying ectoderm. These may indicate that at one time this encephalomere was a region of cell proliferation and thus possessed a neural crest; but since the cells soon disappear, and since no new ones take their place, this encephalomere may be said to be a region of the neural tube which now (in *S. acanthias*) possesses no neural crest. That portion of the neural crest which arises anterior to this neuromere has been variously called "Trigeminus Anlage," "germe du

¹ A study of the histogenesis of nerve has been made only in the case of the eye-muscle nerves, whose morphology still remains a matter of much dispute.

² I am surprised by Hoffmann's ('94) statement that in *S. acanthias* the trigeminus Anlage first appears in an embryo with 17 somites, that is, after the closure of the neural tube.

Trijumeau" (Mitrophanow, '93), and "erste periaxiale Strang" (Goronowitsch, '93). Its cells at this stage (15 or 16 somites) have already migrated half way down the side of the neural tube (Fig. 7). In the region of encephalomere V the disassociation of the cells of the neural crest has begun, and the dorsal part of the encephalomere in consequence appears enlarged. A ventral migration of its cells, however, does not take place until a later stage.

In an embryo of 18 or 19 somites (Plate 3, Fig. 8) two regions of cell proliferation, separated sharply by encephalomere IV, are seen. Mitrophanow ('93) has stated that at the beginning the facialis is not wholly separated from either the trigeminus or the vagus group. I find on the contrary, as already stated, that no neural crest is found in the region of encephalomere IV, and that consequently the "Trigeminus Anlage" is separated by the space of this encephalomere from the posterior portion of the neural crest. Apparently as a consequence of cell proliferation and migration, the dorsal wall of encephalomere III is very thin at this stage, while that of encephalomere IV is considerably thicker and its cells are more compactly arranged. The cells of the neural ridge which form the "Trigeminus Anlage" now extend ventrally as far as van Wijhe's second somite. The second region of cell migration is at this stage sharply confined to encephalomere V. Behind this a disassociation of neural-crest cells has begun in the region of encephalomere VI, but no migration has taken place. From an examination of later stages, the cells proliferated from the region of encephalomere V are easily proved to pass ventrally into the hyoid arch, and to form the ganglionic Anlage of the acustico-facialis. From a study of mitotic cells and from the grouping of cells one is led to believe that the greatest cell proliferation takes place in the posterior part of this neuromere.

It is to be noticed that the advancing ventral end of the ganglionic Anlage extends toward the cleft between van Wijhe's third and fourth somite. Also that cell processes from each of these somites now extend toward the ganglionic Anlage.

When the embryo possesses 19 or 20 somites (Plate 3, Fig. 9) the "Trigeminus Anlage" shows a differentiation into an anterior smaller portion, which passes in front of the midbrain vesicle toward the optic evagination, and a posterior larger portion, which extends ventrally into the mandibular arch, just beneath the superficial ectoderm and external to the second somite. I am inclined to believe that this division of the Anlage is partly due to the enlargement of the vesicle of the midbrain, since frontal sections show that the lateral wall of the midbrain lies very

close to the ectoderm. It is evident that the neural-crest cells migrate around the most expanded portion of the vesicle, so that they come to lie in the regions of constriction anterior and posterior to the dilated vesicle. They migrate, as it were, into the spaces where there is room for them. The cells of these two portions are in continuity dorsally, as in the previous stage. As a result of the expansion of the dorsal wall of the neural tube in the region of encephalomere III, the cells of the neural crest are laterally displaced in this region, so that they appear in optical sagittal section (Fig. 9) to have taken a more ventral position. Mitrophanow ('93) has given the name "le groupe nerveux antérieur" to the anterior smaller portion of the trigeminus Anlage, and states that "dans la plupart des cas, ce groupe est peu séparé" (i. e. from the "groupe du nerf trijumeau"). Coggi ('95) finds that in *Torpedo* this anterior portion of the trigeminus Anlage arises as a paired structure, the lateral halves of which secondarily unite in the mid-dorsal line; Coggi, however, agrees with Mitrophanow that this anterior part of the trigeminus is at first distinct from the posterior larger portion. In *S. acanthias*, however, I find that both anterior and posterior parts form at first a continuous neural ridge, which lies dorsal to the midbrain vesicle. Only in later stages does the anterior portion become separated as the so called thalamic nerve. At the stage with 19 or 20 somites the cells proliferated from encephalomere V extend somewhat farther ventrad toward the hyoid arch than in the preceding stage, and at the same time a proliferation of cells from the mesoderm extends dorsad to meet them. The mesodermal cells migrate from both sides of the constriction between van Wijhe's second and third somites, and from them extends a cellular process toward the ganglionic Anlage.¹

The conditions remain practically unchanged in a stage with 21 or 22 somites (Plate 3, Fig. 10). The anterior and posterior portions of the trigeminus Anlage now extend into the region ventral to the midbrain vesicle, and are about to unite with each other. The cells in the region of encephalomere III have undergone a still greater lateral displacement, from which one may infer that cells are no longer proliferated from the neural crest of this encephalomere. It is seen that the cells of the acustico-facialis are now united with the cellular process from the

¹ I have been unable to determine that these mesodermic cells participate in the formation of the Anlage of the nerve. It appears to me, however, that such a response on the part of the somites to the development of a nerve Anlage is a fact which cannot be ignored in dealing with the question of nerve development. See also similar evidence in the description of the development of the trochlearis and oculomotorius.

mesoderm.¹ This process may be traced dorsally to a point outside of the ganglionic Anlage, i. e. between it and the superficial ectoderm. The future course of the nerve is along the line of the process. Between this and the next succeeding stage, which is represented in Figure 11, the trigeminus Anlage undergoes a considerable change. The anterior (thalamic) and posterior (trigeminal) portions having fused ventrally below the lateral midbrain swelling, now extend ventrad as a continuous sheet with two ventral processes, one reaching into the mandibular arch and the other to a point below the eye vesicle. The anterior (thalamic) portion has assumed a more compact appearance, and extends from the region of the constriction between forebrain and midbrain, both ventrad, to a point above and behind the eye vesicle, — where, as already stated, it meets the anterior prolongation of the trigeminus portion, — and anteriorly to a point in front (dorsad) of the eye vesicle. The acustico-facialis Anlage now extends into the hyoid arch, *its position being clearly inter-somitic*. Posteriorly, in the region of encephalomere VI, and to a considerable extent behind this, the cells of the neural crest have begun their ventral migration. At this time, then, a continuous neural ridge or crest extends from the anterior boundary of encephalomere V backward into the region of the spinal cord. In cleared specimens and in parasagittal sections the neural crest cells seem discontinuous in the region of constrictions between encephalomerer IV, V, and VI. Both Rabl ('92) and Hoffmann ('94) have held that the pre-auditory portion of the neural crest is discontinuous with the post-auditory portion, and Rabl considers this another proof that the pre-auditory region is one "sui generis." On the other hand, Dohrn ('90) and Mitrophanow ('93) have stated, like the present author, that they find the crest continuous in the two regions. 7

A well marked proliferation of cells seems to take place in the region of encephalomere VI. These cells may be traced continuously into later stages, until they enter the first branchial arch and form the Anlage of the glossopharyngeus. Since previous investigators, with the exception of Herrick and Broman (see Table II., p. 152), have stated that the glossopharyngeus is related to hindbrain neuromere VII,² it seems well to call attention to the fact that the cells of the ganglionic Anlage of this nerve ✓ x

¹ Is this mesodermal process the median branch of Kupffer's typical segmental nerve? Its relation to the mesoderm leads me to believe that this is the case. It soon disappears, as stated by Kupffer ('91).

² Miss Platt ('89) stated that the glossopharyngeus is connected with the posterior constriction of encephalomere VI.

are proliferated from the region of encephalomere VI, the greatest proliferation occurring, however, as in the case of encephalomere V, in the posterior part of the encephalomere. No previous observer has stated that the cells of the ganglionic Anlage of the ninth nerve are proliferated from encephalomere VI. However, that previous observers have seen the proliferation of cells from this encephalomere is possibly shown by the fact that both Shipley ('87) and Kupffer ('94) have found in *Petromyzon*, between the Anlagen of the 7th and 9th nerves, a "weak primitive acusticus, which soon vanishes." Hoffmann ('94) stated that in *Acanthias* embryos with 32 to 35 somites, a new outgrowth appears between the facialis and the glossopharyngeus, which to all appearance is a rudimentary and early aborting segmental nerve. Although Hoffmann published no figures, I infer from his description that this outgrowth, or rudimentary nerve, is that portion of the neural ridge which is proliferated from the region of encephalomere VI. I am at least able to say positively that no other outgrowth of cells takes place just posterior to the Anlage of the acustico-facialis. In the phenomena presented by this outgrowth Hoffmann finds the chief support for his contention that the Anlagen of cranial nerves arise as paired segmental outpocketings of the neural tube, corresponding to, or comparable with, the outgrowth of the eye vesicles. He figures diagrammatically the outgrowth of the neural crest in the region of the glossopharyngeus Anlage as an outpocketing of the dorsal wall of the neural tube possessing a lumen continuous with that of the tube. At no time do I find evidence of a lumen between the neural-crest cells, although in later stages the nuclei in the VII and IX ganglionic Anlagen tend to take a peripheral position.

At a stage with 26 or 27 somites (Plate 3, Fig. 12) the thalamic portion of the trigeminus Anlage is no longer continuous dorsally with the posterior portion of the Anlage, the cells of which come to lie in the region of constriction between midbrain and hindbrain. The thalamic portion extends from the constriction between primary forebrain and midbrain toward the eye vesicle, just behind which it unites with a line of cells, ectodermal in origin, which extends along the dorsal border of the eye close to the superficial ectoderm. Some of the cells of the trigeminus Anlage now extend into the mandibular arch, and have there come to surround the mandibular mesoderm.

A displacement of the cells of the Anlage of the acustico-facialis and of the glossopharyngeus has begun at this stage. This is clearly to be accounted for by the invagination of the auditory epithelium, which is now

beginning opposite encephalomere VI. In parasagittal sections the Anlage of the glossopharyngeus appears clearly distinct from that of the vagus, while in the median plane they are seen to be continuous portions of the neural crest.

When the embryo has 28 to 30 somites (Fig. 13) the conditions, so far as the trigeminus is concerned, are practically unchanged. Neural-crest cells still persist in the regions of constriction between the primary brain vesicles. Thus, three strands of neural-crest cells are seen to lie in the region of constriction between the brain vesicles, just as they do in the trunk between the myelomeres. The ganglionic Anlage of the acustico-facialis, which had fused with the thickened auditory epithelium in the early stages of its development, now, as the nerve Anlage recedes from the ectoderm, retains this connection, forming thus the Anlage of the acusticus. The acusticus therefore in its development and relations resembles a *ramus dorsalis* of a cranial nerve.

The cells of the glossopharyngeus have been further displaced. In all the specimens of this stage which I have examined, two distal portions of the nerve Anlage may be distinguished. The fate of the posterior of these is unknown to me. The cells of the anterior portion pass ventrally into the third visceral arch, and are related to the constriction between van Wijhe's somites 4 and 5. In precisely the same way the Anlage of the seventh nerve occupies the cleft between the third and fourth somites. The advancing ganglionic Anlagen pass close to the superficial ectoderm in the plane of the constrictions between the somites. Similarly the Urvagus Anlage meets the mesoderm at the posterior cleft of the fifth somite. This fact seems to me to be of some importance in considering the question whether the branchial nerves are somitic or intersomitic in position, and to warrant the conclusion that the cranial nerves resemble the dorsal nerves of *Amphioxus* in being intersomitic, as well as in other respects. At a stage with 33 or 34 somites (Plate 3, Fig. 14) the trigeminus Anlage retains connection with the mid-dorsal line of the neural tube in only two restricted regions, anteriorly by the "thalamic" portion, and posteriorly (in the region of the constriction between midbrain and hindbrain) by a strand of cells to which Miss Platt has given the name "primary trochlearis." Posteriorly the cells of the trigeminus Anlage are grouped into a somewhat thickened mass opposite the posterior part of encephalomere III, the first indication of the differentiation of the Gasserian ganglion. The Anlagen of the acustico-facialis and the glossopharyngeus have become farther separated by the invagination of the auditory epithelium, the displacement affecting the cells of

the glossopharyngeus so much that they now lie opposite encephalomere VII. The two nerve Anlagen, however, usually remain connected with each other dorsally by a thin cellular strand. This strand is wanting in some cases, or may be present on one side of the embryo only. Dohrn ('90) has also stated that the separation of the seventh and ninth nerves is due to the crowding caused by the ear capsule, and he held that the connecting strand of cells was evidence of the original continuity of the neural crest on the dorsal side of the ear. Behind the glossopharyngeus the neural crest extends in unbroken continuity into the trunk, but only its anterior portion, which forms the ganglionic Anlage of the Urvagus, extends ventrally between the mesoderm of the side plates and the superficial ectoderm into the region of the pharynx.

In embryos with 38 or 39 somites (Plate 3, Fig. 15) the thalamic portion still extends as a compact cellular cord from the region of constriction between forebrain and midbrain to a point above the eye, where it unites with the line of ectodermal cells which in later stages forms the ophthalmicus profundus trigemini. This nerve, because of its relations with the trigeminus, "primary trochlearis," and "thalamic" nerves, is regarded by Marshall ('82) and Miss Platt ('91) as a commissural nerve connecting the three nerves mentioned. It has also been regarded as an independent nerve (van Wijhe, '82, M. Fürbringer, '97), and as a ramus dorsalis either of the trigeminus or the oculomotorius. The acustico-facialis Anlage, opposite encephalomere V, is still in continuity with that of the glossopharyngeus by means of a cellular cord dorsal to the auditory invagination, while the cells of the glossopharyngeus and vagus Anlagen no longer appear to be continuous dorsally, as they were in the previous stage.

At a stage of development when the embryo possesses 42 to 44 somites (Plate 3, Fig. 16), and when two visceral clefts are formed, both the thalamic and trochlear portions of the trigeminus Anlage are much reduced. In an embryo with 48 somites the thalamic portion consists of a strand or cord of cells which extends dorsally from the ophthalmicus profundus, at a point just above the eyestalk, toward the region of constriction between primary forebrain and midbrain, where the two cellular strands coming from opposite sides of the head unite above the wall of the brain. Because of this union, Coggi ('95) has considered this portion of the trigeminus Anlage as a connective "nerve," uniting the *lateral halves* of the ophthalmicus profundus. Its position in *Torpedo*, according to Coggi, is anterior to the thalamencephalon. If Coggi is correct, its position in *Torpedo* is clearly different from that

in *S. acanthias*. Coggi's account differs, however, from that of Dohrn ('90*), who found its relations in *Torpedo* to be similar to those described by Miss Platt ('91) for *S. acanthias*. The relations of the acustico-facialis and glossopharyngeus remain unchanged. For a long time cellular strands persist, showing the primitive relation of these nerves to the constrictions between the encephalomeres IV, V, and VI, respectively.

Some important changes in the relations of the neural-crest cells appear in the next (48-somite) stage, and are shown in Plate 3, Figure 17. For the first time, we find "fibrillar" connections of the trigeminus Anlage with the neural tube. Protoplasmic or fibrillar processes extend from the cells which lie opposite the constriction between encephalomeres III and IV toward both encephalomeres. It has been stated by some investigators (Miss Platt, '91, Locy, '95), that this nerve has its origin from the constriction between the neuromeres. Two main roots are differentiated later, an anterior, in relation with encephalomere III (the "portio minor"), and a posterior, in relation with encephalomere IV (the "portio major"). The nearness of the ganglion cells to the brain wall renders it impossible for me to determine in which direction, whether toward the brain or toward the ganglion, the fibres are first developed. The two chief roots of the trigeminus have been described for other Vertebrates.

The thalamic and trochlearis portions of the trigeminus Anlage are now much reduced in size, each retaining connection with the rest of the nerve fundament by means of an attenuated protoplasmic fibre. The acustico-facialis Anlage has assumed fibrillar connection with encephalomere V, with which it remains connected until the encephalomere disappears. Marshall and Spencer ('81, p. 481, '86, p. 100) have stated that in *Scyllium* "there is an important difference between the fifth and seventh nerves, inasmuch as in the former the primary root is lost and the secondary alone retained, whilst in the latter both primary and secondary roots are retained up to stage N, and indeed . . . throughout life. The difference between the roots of the fifth and seventh nerves just noticed does not occur in the chick." They also state that in early stages in *Scyllium* embryos the fifth nerve arises from the brain by three distinct roots, but that in later stages only two roots are found. Their distinction between primary and secondary nerve "roots" is obviously unnecessary, since the only true "roots" are the so called secondary ones. Before these are established we have to do with neural-crest cells, some of which have been shown to be non-nervous

in function, and to contribute to the mesenchyma of the head.¹ The ear capsule now lies with only its anterior portion opposite encephalomere VI. Behind the ear capsule and opposite the posterior portion of encephalomere VII lie the cells of the glossopharyngeus, as yet without fibrillar connections with the neural tube. Behind the glossopharyngeus and now separated from it lie the cells of the vagus, extending ventrally as a broad sheet between the mesoderm and ectoderm into the region of the pharynx, where the Anlage becomes segmented by the formation of the visceral clefts. The trochlear and thalamic portions of the trigeminus soon disappear without assuming fibrillar relation with the neural tube.

At a stage with 52 somites, when the embryo is about 8 mm. in length, the thalamic portion remains as a group of cells lying in the constriction between the forebrain and midbrain vesicles (Plate 4, Fig. 18), but without connection with the ophthalmicus profundus. It very soon disappears entirely, and I think probably contributes to the loose mesenchyma of this region. In precisely the same way the disassociation of cells of the trochlear portion takes place, scattered clumps of cells indicating its previous extent. The Gasserian ganglion and the ganglion of the ramus ophthalmicus profundus (mesocephalic ganglion) are both clearly differentiated. Three branches of the fifth nerve may now be distinguished, viz. the two sensor branches, r. ophth. profundus and r. maxillaris (inframaxillaris² Dohrn), and the mixed mandibular branch. Nerve relations to the neural tube remain the same as in the previous stage.

d. DEVELOPMENT OF THE

1. OCULOMOTORIUS.

By the time the embryo has reached the length of 8 mm. (52 somites), the oculomotorius has however appeared as a fibrillar process from the base of the midbrain (encephalomere II, Figures F to H), arising as processes from neuroblast cells in the ventral horn of this encephalomere. Since this nerve throws light on the morphology of the pre-mandibular somite, whose musculature it innervates, its development is of great interest and has been studied by many investigators; viz. Marshall ('81), Rabl ('89), Dohrn ('91), Platt ('91), Mitrophanow ('93), and Sedgwick ('94). Neither Marshall ('81) nor Rabl ('89) saw the

¹ Kastschenko ('88), Goronowitsch ('92), Miss Platt ('93).

² This is, I believe, the nerve which in *Ceratodus* van Wijhe ('82) named ramus maxillaris superior, which in *Amphibia* Strong ('95) called accessory branch of the fifth, and Miss Platt ('96) r. buccalis profundus V.

early stages of its development, and their conclusions are therefore purely theoretical. Both agree in considering the nerve a derivative of neural-crest cells. Rabl ('89, p. 221) thinks he has some right to bring this portion of the neural crest into genetic connection with these nerves, since the course of the third and fourth nerves in later stages corresponds with a portion of the trigeminus Anlage, which I infer from his description to be the "trochlear" portion. He adds, "Ferner darf ich



FIGURE F.

aus einer Reihe von Beobachtungen, die ich nicht bloss an Selachiern, sondern auch an Vögeln und Säugethieren angestellt habe, schliessen, dass die Oculomotoriuswurzel, die nach dem gesagten Anfangs ebenso wie die des Trochlearis aus der dorsalen Kante des Mittelhirns austreten musste, aus dieser Lage allmählich durch die Ausbildung der Pedunculusbahnen verdrängt und an die ventrale Seite verschoben wird."

FIG. F. Left face of a parasagittal section through the left half of an embryo with 52 somites, showing the relations of the oculomotorius to encephalomere II at this stage. $\times 50$. I, II, III, first, second, and third encephalomeres; 1, 2, van Wijhe's first and second head cavities; a, ventral fibre tract; oc-mot., oculomotorius; vn. crd., anterior cardinal vein.

More theoretical and farther from the truth Rabi could scarcely be, yet several investigators have in essential respects confirmed his theory, that the oculomotorius is a derivative of the neural crest. Dohrn's ('91) observations, however, differ fundamentally from those of his predecessors. He sees the beginnings of the oculomotorius in embryos intermediate between Balfour's stages I and K. At first cells in the base of the brain assume a more transparent appearance, and later migrate into the "Randschleier," where they send out processes which unite in a network just outside the base of the brain to form the stem of the nerve. Immediately at the beginning of the outflow of the plasma

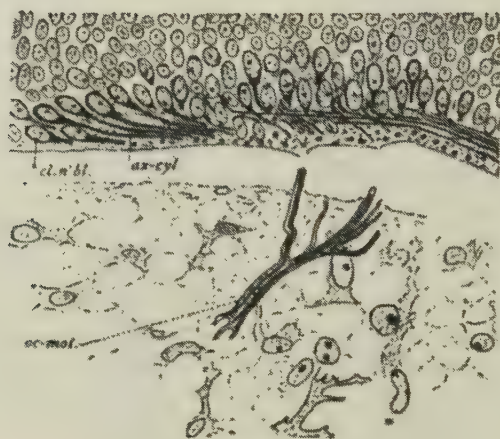


FIGURE G.

cells are seen half in and half out of the wall of the tube, and later, but before the oculomotorius has any connection with the mesocephalic ganglion, large deeply staining nuclei are seen in the protoplasmic network which forms the root of the nerve. Dohrn does not lay great stress on the fact that these nuclei are larger than those of the surrounding mesenchyma cells, but from the fact that similar nuclei lie nearer the medullary wall, from which they appear to emerge in increasing numbers during the course of development, he holds the opinion to be permissible, that the nuclei of the early network are emerged medullary elements, and not mesoderm cells which press close to the medullary

FIG. G. A portion of the same section as that shown in Figure F. $\times 240$. The fibrillar nature of the oculomotorius is clearly shown. *ax-cyl.*, axis cylinder process; *cl. n'bl.*, neuroblast cell; *oc-mot.*, oculomotorius.

wall. Dohrn considers it as the *punctum saliens* of the evidence given by him, that ganglion cells and ganglia which may be traced to the adult are to be found in the course of the oculomotorius before this comes into connection with the mesocephalic ganglion, and concludes that such ganglion cells can have had no other source than the ventral horn of the midbrain. He thus takes the view of Balfour, Marshall, Kupffer, and others, that this ventral nerve is formed as a chain of medullary cells, in opposition to the views of His ('89), Kölliker ('92), von Lenhossék ('92), and others, that ventral nerves are formed from *processes* of "neuroblast" cells in the ventral horn of the medullary tube.

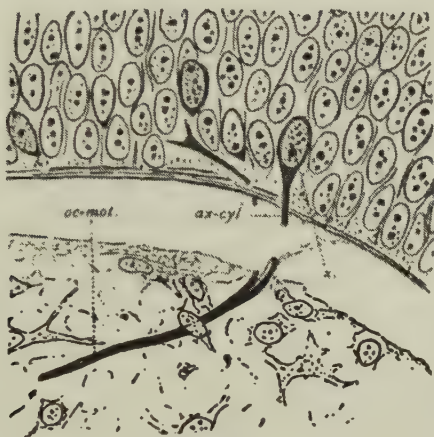


FIGURE H.

Miss Platt ('91) comes to fundamentally different conclusions from those of Dohrn ('91). She finds that the oculomotorius appears first as a single cell proliferated from the mesocephalic (ciliary) ganglion toward the base of the midbrain, with which it at first has no connection. Observations on *Squalus*, *Raja*, *Pristiurus*, and *Torpedo* convince her that the oculomotorius develops after the type of a sensor nerve [?] by a proliferation of ganglion cells toward the brain wall. Mitrophanow's ('93)

FIG. H. Left face of a parasagittal section through the right half of the same embryo as that represented in Figures F and G, showing the oculomotorius in an early stage of development (52 somites). $\times 447$. The relation of the nerve fibre with an axis-cylinder process from the neuroblast cell *x* seems clear. *ax-cyl.*, axis-cylinder process; *oc-mot.*, oculomotorius; *x*, neuroblast cell.

observations confirm those of Miss Platt. According to Sedgwick ('94) the third nerve is formed directly from the neural crest as are the dorsal cranial nerves [?], but arises as a differentiation of the reticulum formed by the breaking up of the neural crest, and first makes its appearance as a projection of nuclei from the mesocephalic ganglion. His observations thus do not essentially differ from those of Miss Platt, their conclusions differing chiefly by reason of difference in theoretical views as to the mode of nerve development. My own evidence differs quite fundamentally from that given by previous investigators, since I find that the nerve develops after the manner described for spinal ventral nerves in *Selachii* and other Vertebrates, as an axis-cylinder process from "neuroblast" cells in the ventral horn of the midbrain. At the earliest stage in which I have been able to detect the oculomotorius the extent of its development and its relationships are such as are shown in Figures F to H, which represent sagittal sections of a *Squalus* embryo with 52 somites (approximately 8 mm. long). At this stage the thalamencephalon is just becoming differentiated from the primary forebrain (encephalonere I). The identification of the fibrillar process as the oculomotorius is made easy by a comparison of its point of attachment, of the direction of its long axis, and of its histological appearance with those of an embryo with 54 somites, where the oculomotorius is already connected with the mesocephalic ganglion. Under higher powers of the microscope the nerve appears as a deeply staining, highly refractive process, clearly distinguishable by these characteristics from the granular and faintly staining processes of the mesenchyma cells at the base of the midbrain. Owing to a shrinkage, which however appears in very few of the specimens killed by the fixing agent used (vom Rath's fluid) and always most markedly in the region ventral to the midbrain, the mesenchyma cells and the roots of attachment of the nerve have broken away from the base of the brain. Since, however, similar deeply staining processes are seen to extend from cells in the ventral horn of the medullary tube towards the points where the roots may be supposed to have once united with the wall of the brain, the inference seems warranted that the nerve is made up of the processes of these cells. The latter show the characteristics described by His ('89) for the neuroblasts of the spinal cord, viz. a highly chromatic nucleus surrounded by a thin, very deeply staining protoplasmic ring, which is prolonged into the axis-cylinder process. The precipitation of osmium serves to render the processes quite opaque and easily traceable among the remaining, as yet undifferentiated, cells of the medullary wall, and to make it possible

to determine that other processes, instead of leaving the medullary wall, extend posteriorly in the wall and parallel with it to form the ventral fibre tract. The nerve process (Figure G) shows a differentiation in its distal portion into two deeply staining fibrils surrounded by more faintly staining plasma, the two fibrils dividing distally into three, which enter the fine processes with which the nerve ends. The nerve process on the other side of the same embryo (Figure H) does not, however, show this same evidence of histological differentiation. Here the nerve appears as a highly refractive fibril, and, while having a greater extent than that of its mate of the opposite side, is composed, except at its root, of a single undivided fibril. The connection of this fibril with the axis-cylinder process from a neuroblast cell in the ventral horn seems indisputable, since this passes directly through the limiting membrane at the base of the brain wall, and projects into the shrinkage space directly opposite the chief root of the nerve, as is shown at *ax-cyl.* I have no evidence to offer, such as that stated by His ('88, '89), for Mammals and other Vertebrates, of a migration of the neuroblasts from the "inner layer" of medullary cells, nor do I find any evidence of migration of cells from the neural tube, as stated by Dohrn ('91). I find at this stage neither nuclei connected with the roots of the nerve outside the neural tube, nor such as are half in and half out of the tube.

The connection of the oculomotorius with cells of the mesocephalic ganglion is attained very quickly, and in embryos of 54 or 55 somites has already taken place. At this stage of development, as seen in embryos fixed with the corrosive sublimate-acetic mixture (Davidoff's fluid), the nerve appears (Plate 8, Fig. 58) as a *cellular* strand, which extends from the inner side of the mesocephalic ganglion toward the ventral wall of the midbrain, with which the nerve unites by at least two main roots. To detect the proximal roots as well as the relations of these with medullary cells, sagittal sections are much more favorable than frontal, since the nerve roots are situated one behind the other.¹ The fact that the nerve is several cells in thickness near the ganglion, while its calibre diminishes as it passes toward the brain wall, would naturally, if one were unacquainted with the conditions shown in the embryo of 52 somites, lead to the inference that the growth of this nerve takes place from the ganglion toward the brain (*vide* Miss Platt, '91, Mitrophanow,

¹ Also, for the reason already stated by His ('88', p. 344) for spinal ventral nerves, that "die Wurzelbündel treten in grösseren Abständen aus dem Rückenmark hervor. Jedes Bündel bezieht seine Fasern aus einem entsprechend breiten Bezirk des Rückenmarks. Die Sammlung derselben erfolgt zum Theil noch innerhalb des Markes, zum Theil erst in der Leibeswand."

'93, Sedgwick, '94). It is interesting to compare the phenomena thus observed in specimens prepared by the Davidoff method with those prepared by the vom Rath method, since the latter clearly differentiates the nerve fibrils, and gives the clue as to the meaning of the cells proliferated from the mesocephalic ganglion. Figure I is drawn from a sagittal section of an embryo with 55 somites killed by the vom Rath method, and fortunately so oriented as to show the oculomotorius in its



FIGURE I.

course from the inner side of the mesocephalic ganglion to a point very near the brain wall. The nerve itself is composed of three deeply impregnated fibrils, which near the brain wall are closely united to one another, while peripherally they become separated. Two lightly staining cells with granular protoplasm lie closely adherent to the nerve, and with low powers are indistinguishable from it. Others appear in the process of migration from the mesocephalic ganglion to assume similar relation. Whether these cells become elements of the oculomotorius ganglion, which would thus conform in its mode of development to the type of a sympathetic ganglion,¹ or whether they form the nuclei of Schwann's sheath, I am not at present in a position to state, since I have not been able to trace their fate. It is of course possible that they contribute to both ganglion and sheath. Whether cells from the mesenchyma in this region contribute to both of these ends, seems to me a question of not great morphological importance, since in my opinion these cells are in great measure, if not entirely, derivatives from the neural crest, and thus *ectodermal*, not *mesodermal*, in origin. From the evidence thus stated it is seen that the oculomotorius must be

¹ Many investigators (Rüdinger, Arnold, Gegenbaur, Schwalbe, Hoffmann, Onodi, van Wijhe, Dohrn, Beard, Ewart) have, on histological and embryological grounds, agreed that this ganglion belongs to the sympathetic system.

FIG. I. Sagittal section of a *Squalus* embryo with 55 somites, showing the oculomotorius in its course from the mesocephalic ganglion toward the brain. $\times 477$. The fibrillar nerve and the peripheral nuclei may easily be distinguished. *cl. ms-ce.*, migratory cell from the mesocephalic ganglion; *oc-mot.*, fibres of the oculomotorius.

regarded as from the earliest stages of development a fibrillar nerve formed by axis-cylinder processes of medullary cells, and that it is no more to be regarded as a *cellular* process or *cellular* nerve in its earlier than in its later stages. The unfavorableness for purposes of nerve study of material killed, with the fixing agents commonly used, has been the chief cause which has kept us so long from the true understanding of the method of the development of the oculomotorius in *Selachii*. I was at first disposed to consider as of some morphological importance the fact that in stages of development before the appearance of the oculomotorius a process extends from the mesocephalic ganglion to the premandibular somite (Plate 8, Fig. 61). Its earlier appearance precluding the view that this process has connection with the oculomotorius, I concluded that it furnishes us with evidence of a primitive relation of the ramus ophthalmicus profundus with this somite (Plate 8, Fig. 61). The observations of J. Müller in 1840, P. Fürbringer ('75), Price ('96), and Max Fürbringer ('97), have established that this nerve possesses motor fibres in the Myxinoids, confirming van Wijhe's view of its segmental value. I am, however, not inclined to lay stress on the fact mentioned above as confirmatory of this view, since in later stages (65 somites) I also find a similar process, apparently in connection with the "anterior cavity" (Plate 4, Fig. 19).¹

At a stage with 65 somites (10 mm.) the relations of the trigeminus are unchanged (compare Plate 4, Fig. 19). The r. ophthalmicus profundus trigemini is well differentiated, and shows a marked fibrillar structure, especially clear in embryos killed with vom Rath's fluid. The nuclei seen along the trunk of the nerve are distinctly peripheral in relation to the nerve fibres. The facialis nerve (VII) now possesses four branches, viz. the sensor acusticus branch, connected with the median and ventral side of the otic capsule; the mixed hyoid nerve, innervating the muscles and skin of the 2d visceral (hyoid) arch; the r. ophthalmicus superficialis VII (ophthalmic branch of the 2d trigeminal root of older anatomists), whose sensor fibres develop in close connection with the skin along what in the head corresponds with the dorso-lateral line of the trunk; and the r. buccalis VII (incorrectly called supramaxillaris V by Wiedersheim), developing along the medio-lateral line of the head.

¹ Allis ('97, p. 742) also describes in *Amia calva* a small and apparently degenerating nerve in connection with the ganglion of the profundus. He however, on grounds of the topographical relation of the eye-muscle nerves (III and IV), regards this nerve as homologous with the ophthalmicus profundus trigemini.

The glossopharyngeus is now in fibrillar connection with the lateral walls of the neural tube at a point behind encephalomere VII. The fibres from the ganglion cells of the vagus enter the neural tube at a point somewhat behind the point of origin of the glossopharyngeus. The cells of the two nerve Anlagen, however, still appear continuous. Posteriorly, and at the same level as the origin of the roots of nerves IX and X, the neural-crest cells appear as a commissure (*coms. d.*) connecting the vagus Anlage with the ganglia of the dorsal spinal nerves. Ventrally the vagus divides into four mixed (post trematic) branches, each of which innervates the skin and musculature of a visceral arch, and posteriorly is continued beneath the skin as the ramus lateralis vagi along the medio-lateral line.¹

At this stage, I find the first evidence of the olfactory nerve (I) in the form of connecting strands or fibres between the anterior lateral wall of the forebrain (prosencephalon) and the thickened lateral epithelium of the olfactory plate. The connection between the median portion of the "Riechplatte" and the brain wall (neuropore) has disappeared at a somewhat earlier period (8-9 mm.). According to Marshall ('78) and Beard ('85) the olfactory nerve develops, as do the other dorsal cranial nerves, from cells of the neural crest, and is therefore regarded by them as a nerve morphologically comparable with the dorsal cranial nerves. The evidence given by van Wijhe ('86*) and Hoffmann ('96), however, serves in the opinion of these investigators to render this view improbable. Van Wijhe ('86*, p. 680) states that "das Riechorgan und der Nerv entstehen beide aus dem vorderen Neuroporus. Der Olfactorius entwickelt sich nicht aus der Nervenleiste, denn er tritt in einer Periode auf, wann dieselbe im Kopfe schon längst geschwunden ist; auch ist er von Anfang an mit der Haut in Verbindung und unterscheidet sich durch diese zwei Merkmale von allen übrigen dorsalen Nervenwurzeln. Der Riechnerv entsteht also erst nach dem Acranienstadium und in Uebereinstimmung damit ist seine Abwesenheit beim Amphioxus."

Confirmatory of this view is the evidence given by Hoffmann ('96, p. 272) that "der Riechnerv fehlt [in Squalus] aber bis zu diesem Entwicklungsstadium [10-12 mm.] noch vollständig und erst bei Embryonen, welche eine Länge von 13½-14 mm. erreicht haben, beginnt er sich anzulegen. Bis zu dieser Periode liegt die Riechgrube der Medullar-

¹ Squalus possesses no dorso-lateral line nerve corresponding with that of Cyclostomata, Dipnoi, and Ganoidei. I also find no evidence in Squalus such as that found by Miss Platt ('94) in Necturus, to show that there once existed a ventro-lateral line in Vertebrates.

wand immer noch unmittelbar an, dies ist auch jetzt noch grösstentheils der Fall, aber mit ihrem medialen Rand fängt sie jetzt an sich von der Gehirnwand zurückzuziehen, bleibt aber mit ihr durch einen kurzen, dicken Zellstrang kontinuierlich verbunden. Dieser Zellstrang bildet die Anlage des Nervus olfactorius, aber es ist nicht möglich zu sagen, welchen Antheil die Epidermis und welchen das Gehirn an der Anlage der Riechnerven nimmt, denn er entsteht aus dem letzten Rest des kontinuierlichen Zusammenhanges von Epidermis und Medullarwand, welcher von Anfang an bestanden hat."

His ('89) had previously found in the human embryo that the first step in the formation of the olfactory nerve was the migration of mesenchymatous cells between the olfactory plate and wall of the brain. Later the olfactory ganglion is formed by the migration of cells from the lateral walls of the olfactory epithelium. Finally, the olfactory nerve results from the assumption by these cells of a bipolar form and the elongation of the poles both centripetally and centrifugally to form fibrillar connection with brain and olfactory pits.

My own observations concerning the development of the olfactorius are as yet incomplete, and I am not able to add much to the evidence which has been given. In agreement with Hoffmann ('96) I find that, as the olfactory plate and the brain wall separate, they retain connection with each other by faintly staining fibrils in the region of the future olfactory pits. Whether these fibrils enter into the formation of the definitive olfactorius I am not able to state, and the observations of Hoffmann appear to me insufficient to establish this fact. My results and those of Hoffmann do not agree; for he finds in embryos of 16 mm., and still more clearly in embryos of 18-20 mm., that *mesenchymatous* tissue "schiebt sich von allen Seiten zwischen Medullarwand und basale Nasen grubewand ein, und in demselben Grade als beide sich entfernen, nimmt natürlich der Riechnerv an Länge zu." I infer this mesenchymatous tissue to be the same as that which Hoffmann previously states to be derived from the "anterior head cavities." My observations, however, lead me to agree with Marshall ('78), that the cells which appear between the nasal pit and the brain wall, as these separate, are neural-crest cells. Van Wijhe may be technically correct in stating that the neural crest has disappeared in the region of the forebrain at the time when the olfactory nerve is established; but it is certainly not true that the neural-crest cells in the region of the forebrain have done so at this stage. They persist in the region of the forebrain which lies opposite and anterior to the optic vesicle, and in my opinion are the cells which migrate between

olfactory pit and brain wall as these separate from each other. I regret that I am not yet in position to describe the later differentiation of these cells, but it appears to me not improbable that they enter into the Anlage of the olfactorius. The evidence given by many histologists, from Schulze to Retzius, establishes the ganglionic character of the olfactorius; while the evidence presented by His ('89*) appears confirmatory of the view of Beard, that the olfactory plate is to be regarded as the anterior of the sense organs of the lateral line, since from it are derived, at least in part, the ganglionic cells of the olfactorius. Therefore, if neural-crest cells also entered into the Anlage of this nerve, it must be regarded as homodynamous with the sensor component of a dorsal segmental nerve.

2. ABDUCENS.

Another of the eye-muscle nerves, viz. the abducens, is now (65 somites, 10 mm.) differentiated. (Compare Figs. 20 and 21 with Fig. 19.) The latter nerve has arisen as an outgrowth from neuroblast cells in the ventral horn of encephalomere VII, and its roots retain connection with this encephalomere until the latter disappears. Zimmermann ('91) stated incorrectly that its connection in *Squalus* is with the neural segment which corresponds with my encephalomere VI. Dohrn ('90*) describes the nerve as having its origin from the neural tube opposite the otic capsule, and between nerves VII and IX. Its position in different Vertebrates seems inconstant. Some investigators (Orr, '87, Waters, '92, and Herrick, '92) have stated that in the forms studied by them it arises from the hindbrain neuromere corresponding with encephalomere IV of my figures. In the chick and swine I have found that its roots are in connection with encephalomere VI, whereas in *Necturus* its fibres may be traced from the musc. rectus posterior to a point behind the ear, and thus have, as I believe, their origin from a segment of the hindbrain corresponding with encephalomere VII. At least, in this form, as in *Squalus*, it appears as a post-otic nerve. Dohrn ('91) gave a careful account of the early stages of its development in embryos of various Selachii. He states that the nerve first appears at a stage corresponding with Balfour's stage L, arising by two roots which unite at a short distance from their point of exit from the ventral wall of the neural tube. In *Mustelus* the roots are more numerous than in the other forms examined, there being as many as six on each side of the brain. The roots are directed backward, as in the case of spinal nerves, but later form a network from which arises the stem of the nerve; this runs forward,

parallel to the neural tube, toward van Wijhe's third somite. In later stages the nerve divides into two branches, one passing along the inner side of the somite, and the other along the outer side. At first the nerve root, which appears as a plasma outflow from the neural tube, is of the thickness of one, or at most two, medullary cells. Later the roots increase in thickness, apparently by the continued outgrowth of plasma from the neural tube, as well as by the migration of cells from the ventral horn of the medulla. The larger size and different staining qualities of the medullary cells enabled him to distinguish them from the mesodermal cells in their vicinity. Such (medullary) cells are often found with a part of the nucleus within and a part without the medullary wall. This outflow (migration) of medullary cells takes place also in later stages after the white substance has become quite thick on the side wall of the neural tube.¹

My observations upon the development of the abducens differ from those of Dohrn, as in the case of the oculomotorius, inasmuch as I find the nerve to arise from axis cylinder processes of neuroblasts in the ventral horn of the medulla, and therefore to resemble in its mode of development that of a ventral spinal nerve, as stated by His ('89). At the earliest stage which I have been able to detect the abducens, it possesses but a single root, formed by the processes of several neuroblasts, as is represented in Figure J. The union of these takes place just outside the medullary wall, yet peripherally the nerve appears as a single process with deeply staining axis and a more lightly stained sheath. I find neither at this stage nor in later stages any convincing evidence of a migration of the neuroblast cells from the wall of the neural tube. In later stages of development sections show that *the nuclei seen along the course of the nerve are distinctly peripheral in relation to its fibres*. Even the phenomena presented in sections of embryos fixed with corrosive-sublimate acetic, such as are represented in Figures 62-65 (Plate 9), warrant in my judgment only the inference that the nuclei of the nerve are peripheral, as held by Miss Platt ('91). The darker appearance of the nuclei lying upon the nerve results more from the opaqueness of the nerve than from any peculiar staining properties of the nuclei. During development the number of roots in the nerve increases from one to three or four, the number being variable even upon the two sides of the same embryo. The method of develop-

¹ Since Marshall ('81), van Wijhe ('82), and Miss Platt ('91) never saw the early stages of development of the abducens, it is unnecessary to restate their results in this connection.

ment of the secondary roots is the same as that described for the primary one, viz. as processes from neuroblast cells in the ventral horn. By following the fibres of the roots in the wall of the brain, it is easily ascertained that the motor "nucleus" of the abducens is a very elongated one, as is known to be the case in higher Vertebrates (see Edinger, '96).

The study of the development of the abducens is simpler than that of the oculomotorius, since the nerve never comes into relation with a ganglion, and thus resembles the primitive ventral nerves of *Amphioxus* more than do the ventral spinal nerves. The gradual extension of its



FIGURE J.

fibres through the mesenchymatous tissue at the base of the medulla may therefore be easily followed. It is a matter of some morphological importance, in my opinion, that not all the nerve fibrils extend anteriorly toward the third somite (van Wijhe's), but that in later stages of development, e. g. in embryos with 78–80 somites (Plate 4, Fig. 20), a nerve fibril is seen to pass from the posterior root of the nerve in a posterior direction toward the myotome of the sixth somite, which has at this stage, however, only a few rudimentary muscle fibres. Miss Platt ('91) likewise has mentioned the fact that this nerve also distributes fibres to mesoderm posterior to the third somite (mus. rectus posterior). In the abducens, therefore, we have to do with a post-otic ventral nerve,

FIG. J. Parasagittal section of a *Squalus* embryo with 60 somites, showing the abducens as a fibril formed by the processes of at least four neuroblast cells. $\times 447$. *abd.*, abducens; *cl. n'bl.*, neuroblast cell.

which develops in precisely the same way as do ventral (medullary) spinal nerves, possesses a much elongated motor nucleus in the ventral horn of the medulla, and innervates pre-otic (possibly also in the embryo post-otic) musculature (musc. rectus posterior). These facts seem significant in dealing with the question of the primitive metameric relations of this nerve.

At a stage when the embryo has a length of 17 mm. (78–80 somites) the ramus ophthalmicus superficialis V (Plate 4, Fig. 20; compare Fig. 21) appears as a fibrillar nerve with peripheral nuclei extending from the Gasserian ganglion just dorsal to the point of exit of the fibres of the r. ophth. profundus V, and passing anteriorly close to the ectoderm below the r. ophthalmicus superficialis VII. The relations of these two ophthalmic nerves are therefore such that they have usually been regarded as of the same morphological value, i. e. as rami cutanei dorsales of nerves V and VII respectively. Yet an interesting relation of protoplasmic processes from the r. ophth. sup. V with the myotome of the second somite, such as is represented in Plate 8, Figure 60, has been called to my attention by Miss Platt. Since at this stage of development the fibres of the trochlearis have not appeared, the inference would seem warranted that motor impulses may have primitively passed to this myotome (musc. obliquus superior) through the fibres of the r. ophth. sup. V. Such a supposition, however, is greatly diminished in force, and in my opinion rendered untenable, by the fact that in embryos of 19 mm. — therefore before the fibres of the trochlearis are in connection with the m. obliquus superior — the r. ophth. sup. V shows no longer connection with this muscle (Figure K). The fibres of the anterior root (portio minor) of the trigeminus nerve may now be traced from their origin through the Gasserian ganglion into the mandibular arch, where they give off fibres both to the muscles of the arch and to the skin of its anterior and lateral surface. The fibres appear in large part motor. Since this is the only motor branch of the V, it would follow that the posterior root (portio major) includes chiefly, if not entirely, sensor fibres. It would moreover follow that encephalomere III is chiefly, if not wholly, connected with motor fibres, which may be traced forward to a considerable distance in it to the neuroblasts in the lateral horn, with which they are in connection, while encephalomere IV has chiefly sensory fibres in connection with it. Mitrophanow's ('93, p. 178) evidence is, however, considerably at variance with that just stated. He finds that in an embryo *Squalus* of 18 mm. "la racine du nerf trijumeau est large

et se divise en deux parties (Pl. XIV. Fig. 8) dont les fibres sortent du cerveau en formant différents coins et se croisent ensuite au dedans du ganglion Gasseri; de cette manière le ramus ophthalmicus profundus les reçoit de la partie postérieure; le ramus maxillaris, de la postérieure et de l'antérieure; le ramus mandibularis, principalement de la postérieure." Mitrophanow's results are seen to differ markedly from mine as to the relationship of the fibres of the ramus mandibularis. My results, however, agree with those of His ('88^b, p. 365, Tab. II, Fig. 3) for the human

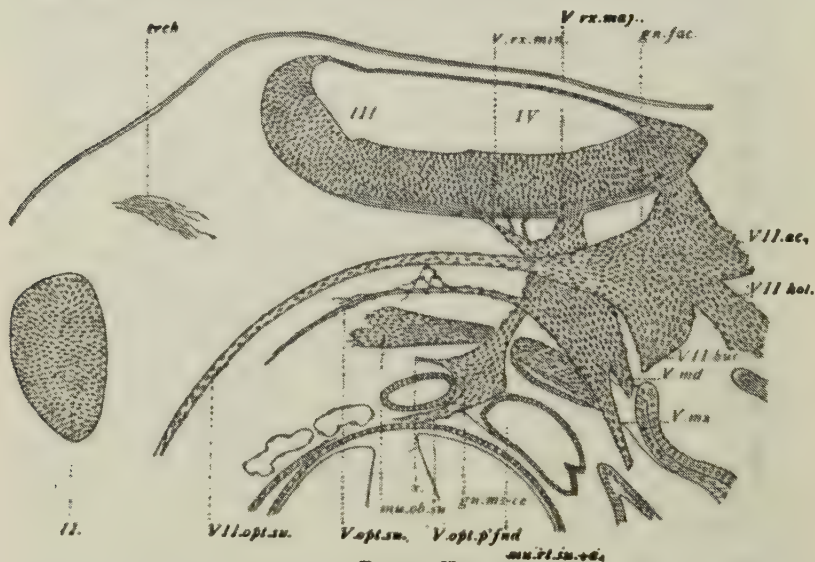


FIGURE K.

embryo. The clear relationship of the motor fibres of the trigeminus with encephalomere III and the visceral part of van Wijhe's second cavity appears to me a matter of considerable morphological importance, and seems to establish the metameric relations of these elements.

FIG. K. Parasagittal section through the left side of a *Squalus* embryo of 19-20 mm. $\times 50$.

II, III, IV, second, third, and fourth encephalomeres; *V. md.*, r. mandibularis trig.; *V. mx.*, r. maxillaris trig.; *V. opt. p'fnd.*, r. ophth. profundus trig.; *V. opt. su.*, r. ophth. superficialis trig.; *V. rx. maj.* and *V. rx. min.*, major and minor roots of the trigeminus; *VII. ac.*, r. acustico-facialis; *VII. buc.*, r. buccalis facialis; *VII. hoi.*, r. hyoideus facialis; *VII. opt. su.*, r. ophth. superficialis facialis; *gn. fac.*, ganglion of the facialis nerve; *gn. ms-ce.*, meso-cephalic ganglion still retaining connection with the ectoderm by the process *x*; *mu. ob. su.*, m. obliquus superior; *mu. rt. su. + a.*, musc. recti superior and anterior (1st cavity); *trch.*, trochlearis.

3. TROCHLEARIS.

In an embryo about 21-22 mm. in length (Plate 4, Fig. 21) the trochlearis, the last cranial nerve differentiated, appears, as stated by Kastschenko ('88, p. 465), in the form of "parallel gehende kernlose und, dem Anschein wenigstens nach, vollständig structurlose Fäden, welche in ihrer ganzen Ausdehnung vom Gehirndach bis zum entsprechenden Muskel verfolgt werden können." The great variety of opinions concerning the morphology of this eye-muscle nerve make interesting the facts of its development. Hoffmann ('89, p. 338), who was the first to study its development, states that in *Lacerta* one finds, as the Anlage of the trochlearis, "einen ziemlich grossen, zelligen Auswuchs" between midbrain and hindbrain. At certain stages the trochlearis possesses "ein sehr deutliches und zwar ziemlich grosses Ganglion, welches aber frühzeitig wieder vollständig abortirt."¹ In later stages of development the trochlear emerges as "dünner, feinfaseriger Nervenstamm von der oben erwähnten Stelle aus dem Gehirn und wird in seinem weiteren Verlauf bald so schwächlich, dass er nur aus einzelnen, sehr dünnen Fasern besteht." In other reptiles, in birds, and in cartilaginous fishes, Hoffmann was unable to find evidence of this ganglion of the trochlearis. In 1890 and 1891 Dohrn announced that, in early stages of the development of the trochlearis, erratic ganglia, which were evidently products of the neural crest, are found in Selachian embryos in connection with this nerve. Whether these ganglia send fibres into the trochlearis stem, he was not able to determine. In later stages anastomosing fibres appear to connect the trochlearis with the r. ophth. sup. V and VII. Moreover, Froriep ('91) thinks he is able to establish in *Torpedo* the genetic connection of a pear-shaped ganglion with the trochlearis. From his studies upon *Torpedo* embryos, he is also forced to conclude that the trochlearis arises *in situ* through the "Umwandlung oder Ausläuferbildung der Ganglienzellen." According to Miss Platt ('91, p. 95), the trochlearis in *Acanthias* first appears as a small fibrous nerve growing from the constriction between midbrain and hindbrain. This may be followed a short distance into the mesoderm, but, becoming extremely attenuated, is soon lost. "Soon after the appearance of this small nerve, which is the root of the permanent trochlearis,² cells are proliferated to meet it from the ganglion cells that

¹ Confirmed by Oppel, '90.

² Miss Platt makes, in my opinion, an unnecessary distinction between a "primary" and a secondary, or "permanent" trochlearis. The "primary trochlearis"

lie above the superior oblique muscle. Thus the permanent trochlearis arises from two sources, from the brain and from ganglion cells." Finally, Kupffer ('91) stated that he had found a nerve in *Ammocetes*, which he thought to be the trochlearis (for reasons not clear to me), directly connected with the second epibranchial ganglion. Were this opinion correct, the trochlearis would be the serial homologue of a branchial (dorsal), not of a spinal dorsal nerve.

From this summary of previous embryological evidence bearing on the question of the morphology of the trochlear nerve, it is clear that little support is given to the view, based on the later histological structure and relations, that it is morphologically a ventral segmental nerve. Only Kastschenko ('88) finds the nerve in early stages fibrillar in structure. The following evidence, however, leads me to conclude that its mode of development is the same as that of the oculomotorius and abducens, and that therefore it must be regarded, like these, as a ventral (medullary) nerve. I first find the trochlearis in sections of embryos of 19-20 mm. as a fibrillar nerve bundle extending from the dorsal constriction between encephalomeres II and III. Two roots are already present at this stage, but neither in these, nor in the nerve bundle as far as its fibres may be traced in the mesenchymatous tissue at the sides of the brain, are nuclei to be found. While proximally the nerve fibres are united in a compact bundle, they distally separate so as to form a loose brush of structureless fibres, which are lost in the mesenchyma at a considerable distance dorsal to the musc. obliquus superior (Figure K). While I am able to offer no direct evidence in favor of the view that the fibres of the trochlearis, as above described, are processes from neuroblast cells in the ventral horn of encephalomere III, I hold that they are such, since their well known later histological relations support this conclusion. Dorso-ventral fibres in this region of the neural tube may indeed be traced in embryos of this stage, but their connection with the fibres of the trochlearis is not clear to me. The dorsal chiasma of fibres is present.¹ Of a ganglion, or of any grouping of cells which might

is that portion of the trigeminus Anlage which I have for convenience called its trochlear portion, which persists for some time in the constriction between midbrain and hindbrain vesicles. Since the proof of its morphological value has not been given, and since the "permanent" trochlearis is not developed from the "primary" trochlearis, as Miss Platt herself states (p. 96), the use of the latter term appears to me apt to mislead.

¹ The explanation for this dorsal chiasma may be sought in some physiological advantage in coördination gained, but it may also be seen that in case the dorsal exit of fibres were of physiological advantage, it would be easy for the fibres to

receive the name of ganglion, there is no evidence at this or later stages. The last traces of scattered groups of neural-crest cells found in some (not all) embryos of earlier stages (17 mm.) have been lost.

In embryos of 21 mm. some of the distal fibrils of the nerve appear to have united with migratory cells from the r. ophth. sup. trigemini, a process in my opinion comparable with that which takes place in the growth of the oculomotorius. At least, in embryos of 21 or 22 mm. the distal portion shows nuclei in relation with the nerve fibres, whereas proximally no nuclei are seen. In still later stages the nerve has a distinctly cellular appearance throughout its length. The nuclei are, however, seen in thin sections to be peripheral in relation to the nerve fibres, as in the oculomotorius (Figure I). The evidence of anastomosis of the fibres of the trochlearis and the r. ophth. sup. trigemini I consider very doubtful. During development the loose brush of fibres at the distal termination of the trochlearis becomes united into a compact nerve stem. It has, therefore, seemed to me that the primary widely spread brush of nerve fibrils may be explained on the ground of advantage gained in seeking the terminal organ, the musc. obliq. superior.

The phenomena observed by me during the development of the trochlearis are seen to correspond very closely with those observed by Miss Platt ('91). To her, as to me, the trochlearis first appears as a fibrillar process from the dorsal wall of the brain. But while she interprets the evidence of cellular growth toward the advancing end of the nerve as of morphological or phylogenetic significance, I am unwilling to give it such interpretation, since I find that these nuclei have nothing to do with the nerve proper. In my opinion, it is probable that they become converted into the nuclei of Schwann's sheath, an opinion which seems confirmed by their peripheral position in relation to the nerve fibres. When the only sections I possessed were of embryos killed with corrosive-sublimate acetic, and stained with carmine or hæmatoxylin, the evidence seemed to me confirmatory of the view of Frierip ('91), viz. that the trochlearis is differentiated from mesenchymatous cells *in situ*. But better methods of preparation have taught me to distrust that evidence, and the results appeared to me too distinctly contradictory to the later histological

cross each other in growth, since the direction of their growth would thereby be unchanged. I assume that it is easier for a nerve fibre to grow in a direct line than to bend back and reverse the direction of its growth. The possibility even of a primary connection of muscle and nerve appears to me to be excluded in the case of the musc. obliq. sup. and the trochlearis.

structure of the trochlearis to be worthy of trust, or even of serious consideration.

Before closing my account of the development of the cranial nerves and their chief branches in *Squalus*, I wish to call attention to a phenomenon seen in still later stages of development, already noted by me in a former paper ('97, p. 455). It appears to me a matter of considerable morphological importance that the ganglion of the dorsal nerve of van Wijhe's eighth somite (fourth post-otic) — the ventral root of which forms at this stage the first of the five hypoglossus roots — unites in late stages of development with the ganglion cells near the root of the vagus. Kupffer ('90) was the first to make evident the morphological importance of the clearly marked distinction between dorsal and lateral (epibranchial) ganglia in embryos of Cyclostomata. While in the embryos of Selachii there is not such a clearly marked distinction, there nevertheless exist at the roots of the vagus groupings of ganglion cells, or at least of neural-crest cells (quite distinct from the lateral, epibranchial ganglia of this nerve, the ganglion nodosum), which in my opinion are to be regarded as homologous with the dorsal ganglion of the vagus of Ammocetes.¹ The evidence of the union of dorsal segmental ganglia in the vagus is as follows. During development the continuous neural crest in the occipital and trunk regions of *Squalus* becomes differentiated into clearly marked ganglia, lying opposite the myotomes and connected by a cellular "dorsal commissure" (Balfour, '81), as far forward in the embryo as van Wijhe's seventh somite. Opposite the sixth and seventh somites no distinct ganglia appear; but instead a wide sheet of cells, lying in close juxtaposition to the extended roots of the nerve, is observable. While in early stages the ganglion of the eighth somite is separated by a considerable interval from the roots of the vagus, in later stages it approaches these, and in embryos of 30 mm. is seen to be in union with them as a well marked ganglionic appendage. In later stages, its fusion appears complete. The ganglion cells do not degenerate, but send axis-cylinder processes both centripetally and centrifugally, the latter forming the posterior of the roots of the vagus nerve. The ganglion of the second hypoglossus root (ninth somite) does not, however, so fuse with the vagus, but is seen in embryos of 50 mm. as a group of cells without nerve relations, so far as I am able to determine, enclosed in the cartilage of the cranium. It apparently disappears in

¹ These are probably the homologues of the intracranial ganglia of Ganoids (see Allis, '97, p. 747).

later stages, as does its ventral root, the hypoglossus of the adult having, according to Gegenbaur ('72) and M. Fürbringer ('97), only two ventral roots without dorsal ganglia. Since the reduction of dorsal and ventral roots takes place from the anterior towards the posterior, these two ventral roots of the adult hypoglossus are in all probability the posterior of the five roots of the embryo.¹ A similar process of fusion of dorsal ganglia with the dorsal ganglion of the vagus takes place in *Petromyzon*; but in that animal the fusion of the ganglion — viz. that of the "spinalartige Vagusanhäng," which for reasons already stated by me ('97, pp. 454, 455) I regard as the exact homologue of the dorsal ganglion of van Wijhe's eighth somite in *Squalus*² — appears by a comparison of the results of Wiedersheim ('80), Schneider ('80), Ahlborn ('84*), Hatschek ('92), Kupffer ('96), and M. Fürbringer ('97) to be a variable one. This union of dorsal spinal ganglia with the ganglion of the vagus, taken in connection with the fact previously stated by me ('97, p. 453), that the dorsal ganglia of the glossopharyngeus and vagus lie *primitively*³ median to the dorsal portion of post-otic somites, is a further link in the chain of evidence which shows that no fundamental distinction between spinal and cranial nerves exists. From the foregoing account it will be seen that, as in the case of spinal nerves, we are able, using as criteria the central and peripheral relationships of the motor fibres, to divide cranial *motor* nerves (roots) into two classes, viz.: (1) dorsal (splanchnic) roots, having their nucleus in the lateral horn of the neural tube and their peripheral distribution in the musculature (ventral) of the visceral arches; and (2) ventral (somatic) roots, which have their nucleus in the ventral horn of the neural tube and their peripheral distribution in the musculature (dorsal) of the somites (somatic muscu-

¹ *Hexanchus* and *Heptanchus* both have five hypoglossus roots in the adult (M. Fürbringer, '97).

² Homologized, however, by Ahlborn ('84*) with van Wijhe's tenth somite, and by Hatschek ('92) with van Wijhe's seventh somite.

³ Goronowitsch ('92) first observed in the chick that the topographic relation of the vagus to the head somites is the same as that of the spinal nerves to the trunk somites. Sewertzoff ('05, p. 92) also states that "Die Beziehung der Kopfmyotome zu den Kopfnerven, z. B. zum N. vagus ist dieselbe, wie diejenige zwischen den Rumpfmyotomen und Rückenmarksnerven, d. h. sie liegen nach aussen von Nerv (*Cyclostomata*, *Ganoidei chondrostei*, *Urodela*, *Reptilia*, *Aves*)."

This is stated, however, by Kupffer ('94, '96) not to be a *primitive* relation of the post-otic myotomes in *Petromyzon*. My own observations and conclusions, however, differ from those of Kupffer (see Neal, '97, p. 453). Miss Platt's ('97) observations on *Necturus*, and her conclusions likewise, confirm the conclusions of Goronowitsch and Sewertzoff.

lature). The motor fibres of nerves V, VII, IX, and X belong to the former, and nerves III, IV, and VI to the latter class.

While it is possible, as has been stated, to establish a numerical correspondence of encephalomeres and somites, the nerve relations are not so clear. We find, for example, that encephalomeres II, III, and VII are connected by ventral (motor) nerves with somites (van Wijhe's) 1, 2, and 3. Such evidence of a want of segmental correspondence would seem at first sight to render untenable the assumption that encephalomeres have the same segmental value as myelomeres. We have already seen that these two classes of neuromeres have structurally little in common. Moreover, a want of correspondence of encephalomeres and visceral arches is shown by the fact that the *dorsal* motor fibres which are connected with encephalomeres III and V innervate two *successive* visceral arches. In view of this discrepancy in the segmental relations of encephalomeres and nerves, can we regard the former of segmental value? Do they afford evidence in support of the assumption that a Vertebrate head segment is comparable, i. e. homologous, with a trunk segment? Before expressing my own opinion in regard to the answer to this question I will briefly review the interpretations given by previous investigators. Two antithetic views concerning the neuromeres have been given, viz. (1) that they are not of segmental or phylogenetic value, and (2) that they are of phylogenetic value.

VII. Segmental Value of Hindbrain Neuromeres.

a. NON-PHYLOGENETIC INTERPRETATION.

In 1877 Mihalkovics, speaking of the foldings in the medulla of birds and mammals, expressed the opinion that the want of correlation between these structures and the nerves and visceral arches seems to favor the view that they are of mechanical origin, i. e. formed by the bending and shoving of the neural tube as it rapidly grows in a confined space. This view seems strengthened by the consideration that the ventral wall of the neural tube of chick embryos is, in early stages, markedly folded into segments, irregular in size and inconstant in appearance, and that these folds in the head region are visibly exaggerated by certain fixing agents which result in shrinking the embryo. Balfour, who with Foster ('74) had been the first to express the opinion that these structures were of phylogenetic significance, afterwards ('81) said that it is uncertain whether they have any morphological significance. In 1892

Froriep, in speaking of neuromeres and their nerve relations, said that these relations are in no way of such a kind that both nerves and neuromeres appear to be constituent parts of a simple organ system. The nerves, especially the trigeminus and facialis, are not so constant in their relation to the folds as would be expected, if the latter were primary segments of the nervous system. It looks much more as if the presence and position of the nerves determines the position of the folds, and as if the appearance of the folds is itself a passive, mechanical one, necessitated by quick growth in length in a confined space. On the basis of his research, he was therefore much inclined to consider these late appearing and transitory segments of the brain as morphologically unimportant phenomena.

Broman ('95) has given a somewhat extended description of the foldings in the hindbrain of a human embryo about three weeks old. Although he nowhere formulates his conclusions as to the significance of the folds, it is evident that he does not regard them as of phylogenetic significance, for he says that the correspondence which earlier investigators have found in their relation to nerves seem to him of little help. In his opinion the results differ too much to allow one to think that a general rule prevails in the Vertebrate series as regards the number and relations of the foldings. The foldings, he says, are intensified in the regions of the greatest flexure of the neural tube, and in these regions the radial arrangements of cells in the foldings is also more marked. This, together with the fact that the foldings are confined to the ventral half of the medulla, harmonizes well with a mechanical explanation of their origin. Upon the evidence that rounded cells (which he thinks are the neuroblasts) with round nuclei may be distinguished in the centre of the most strongly developed parts of the brain foldings, Broman ('95, p. 189) forms an hypothesis concerning the origin of the separation of lateral and ventral roots. He says: "Wenn wir noch einmal alle die oben von mir als Neuromeren bestimmten Falten durchmustern, finden wir, dass nur das als Abducensneuromer bezeichnete die ventrale Wand des Hirnröhres ausbaucht. Alle übrigen sind entweder ganz und gar davon abgedrängt, oder auf dem Wege es zu werden. Dies kann natürlicher Weise ein blosser Zufall bei diesem Embryo sein."

Since Broman's paper is, with the exception of Locy's, the most recent one on the question of neuromeres, I will discuss his evidence and conclusions at some length. It is unfortunate for the purpose of discussion that he has failed to identify correctly the cerebellum Anlage. What he calls Cerebellumanlage is the posterior of the two secondary sub-

divisions of encephalomere III, as may easily be determined by a comparison of his figures with frontal sections of swine embryos. He says (p. 188), "Die ventrale Ausbuchtung der zweiten Falte kann man also mit vollkommene Sicherheit für die beginnende Ponsanlage, und ihren oberen Theil für die Cerebellumanlage halten." But, as may be determined by the relations of the neuromeres to the ear capsule and to the ganglia of the acustico-facialis and the trigeminus in his figures (Taf. X. Figs. 4, 5), the true Anlage of the cerebellum lies anterior to this and is his "erste Falte," which on theoretical grounds he considers related to the trochlearis nerve. As a result of this mistake it happens that the neuromere which he calls "Abducensneuromer" (VI), and to which on purely theoretical grounds he assigns the sixth nerve, is in reality encephalomere V, which is connected with the acustico-facialis. *With this neuromere the abducens never is conneced in any Vertebrate yet studied.* In the swine, as I am able to affirm from my own observations, the abducens arises from the ventral portion of hindbrain neuromere VI, which in the early stages of all Vertebrates lies opposite the ear capsule. In *Necturus*, the chick, and *S. acanthias*, its origin is ventral and posterior to the origin of the acustico-facialis. In support of this theory of the mechanical origin of the "Falten," Broman finds that, as a result, as he thinks, of the flexure of the neural tube, those neuromeres which correspond with encephalomes IV and VI of my figures are wedge-shaped, and that their ventral edges do not reach the ventral wall of the neural tube. Moreover, none of his neuromeres extend to the "Deckplatte." But a study of swine embryos leads me to conclude that this is not characteristic of all mammalian embryos, and indeed that it may be "ein blosser Zufall" in the case of Broman's human embryo. In young swine embryos (killed 19 days after coitus) *none of the neuromeres are wedge-shaped ventrally or dorsally*; moreover, the constrictions between them extend into the Deckplatte. The posterior constriction of encephalomere V extends *across* the Deckplatte until a somewhat later stage, and in this constriction a mass of neural-crest cells persists in a way precisely similar to that in which neural-crest cells in *S. acanthias* persist in the regions of constriction between the primary brain vesicles (encephalomes).¹

From an examination of the evidence presented by those who have held that the neuromeres are purely the result of mechanical influences,

¹ In connection with this fact, it is to be noted that the walls of the medulla in this region are little distended laterally, which may be ascribed to the influence of the ear capsule. (See Plate 5, Fig. 30.)

it is evident that the chief support for the hypothesis consists, first, in an apparent want of a definite relation of the nerves to the neuromeres in the different Vertebrate groups, — i. e. an apparent inconstancy in the structures themselves, — and, secondly, in the fact that the hypothesis seems to explain the structural conditions presented.

I turn now to a consideration of the arguments supporting the view that the neuromeres are of morphological (phylogenetic) importance.

b. PHYLOGENETIC INTERPRETATION.

A phylogenetic interpretation of the foldings of the medulla was first given in 1874 by Foster and Balfour. The following year Dohrn accepted this explanation. Béranek ('84) showed that in the Lizard the hindbrain folds ("replis") were definitely related to certain nerves. Having later ('87) confirmed his observations by studies of chick embryos, he concluded that the foldings are *the last indisputable remnants of the primitive segmentation of the head*. It is notable that he reached this conclusion notwithstanding the fact that, in his opinion, the segments of the spinal cord do not have the same characters as those found in the foldings of the hindbrain. Subsequent investigators, however, have sought to compare encephalomeres with myelomeres. In 1885 Rabl found in chick embryos a regular folding of the side walls of the myelencephalon, the segments of which showed the same characteristics as the foldings in the region of the spinal cord. During the same year Kupffer ('86), in studies on different Vertebrate embryos, found that the foldings extended into the midbrain region. Because of the relatively late appearance of the folds, — "after the closure of the neural tube, after the formation of three brain vesicles, and long after the segmentation of the mesoderm," — Kupffer thought that there was much against the interpretation of these folds as remnants of a primary general metamorphism of the neural tube, but his later observations — previously cited in another connection (p. 174) on an embryo of *Salamandra atra* at a stage before the closure of the neural plate — led him to believe that in this particular case there is a primary segmentation.

The fact that Kupffer here found eight cross furrows in the brain region, representing as many "ancestral segments," appears to have strongly influenced his subsequent interpretations of the morphology of the forebrain in different Vertebrates, for in his later studies he has sought to find evidence of these eight primary "encephalomeres" in the forebrain and midbrain, *even* "after the closure of the neural tube, and the

formation of the three brain vesicles, and long after the segmentation of the mesoderm" ¹

McClure ('89, p. 435, and '90, p. 37) concluded, from studies on embryos of *Amblystoma*, *Anolis*, and chick, "that the symmetrical constrictions or folds found in the lateral walls of the embryonic brain are remains of the primitive segmentation of the neural tube, in part atavistic, extending [from the spinal cord region] into the primary forebrain." The serial homology of the segments of the myelon and the encephalon seemed to him certain, since he found both the structural characteristics and the nerve relations to be the same in the two regions. "The dorsal roots of spinal nerves take their origin from the *apex* of their respective myelomeres in exactly the same manner as the nerves of the medulla do from their respective encephalomeres" ('89, p. 437).

In the same year Miss Platt ('89) also advocated the view that there is a serial homology between the encephalomeres and the segments of the spinal cord. While she agrees with Orr and Béranek in regard to the number and appearance of the neuromeres and the ultimate relations of the nerves, she finds that the cranial nerves develop from the *constrictions* between neuromeres, precisely as the spinal nerves do. In answer to objections to the attempted homology between cranial and spinal segments, she says that in both head and trunk the segmentation is transitory, and that in both regions it is more manifest in the ventral portion of the neural tube.

The conclusions of Waters ('91) are largely confirmatory of those of McClure, viz. that there is a similar segmentation in brain and spinal cord, with similar sensor nerve relations in both these regions.

Zimmermann ('91), as a result of his studies on rabbit, chick, and *Squalus* embryos, thinks he is able to confirm Kupffer's discovery of eight primary cephalic segments or "encephalomeres," although his eight "primäre Abschnitte" include forebrain, midbrain, and hindbrain regions, while Kupffer's theoretical conclusion was that his eight "primäre Medullarfalten" do not include the hindbrain.¹ Although Zimmermann states that the spinal cord does not appear segmented, he finds in later stages thirteen homodynamous "encephalomeres," and has given a table of these with their nerve relations. He supposes three roots, a dorsal, a lateral, and a ventral one, to be related to each encephalomere, but his table gives chiefly the impression of numerous gaps to be filled with hypothetical nerve roots.

Herrick ('92) states that he finds the segmentation of the medulla

¹ At first Kupffer thought they did not include the forebrain!

and spinal cord of snake embryos not explicable on mechanical grounds. "The neuromeres of the medulla cannot be ascribed to the mechanical influence of the Anlagen of the nerves, for those segments which have no nerves develop equally with the others" (cf. Froriep, '91). He considers however "the neuromeres of the forebrain" region wholly illusory from a morphological standpoint, since they involve only dorsal structures.

c. INTERPRETATION OF HINDBRAIN NEUROMERES IN SQUALUS ACANTHIAS.

I believe that the evidence which I have obtained from a study of the development of hindbrain neuromeres in *S. acanthias* excludes the possibility of a simple mechanical explanation of them. In their earlier stages they were seen to be local thickenings of the lateral walls, a phenomenon intelligible only on the ground of unequal growth, and not in the least explicable as the result of the passive bending or shoving of a tube already formed.¹ Since the somites do not extend into the region of the dorsal part of the encephalomeres, the possibility that the neural tube in this region is constricted by them is excluded. They are, then, in both structure and mode of development, clearly not to be explained in the same way as the myelomeres. Again, that they are not due to the effect of the Anlagen of the nerves, as supposed by Froriep, is shown by the fact that encephalomere IV develops equally with the others, although there is no nerve in relation with it until a comparatively late stage. Since the fibrillar connection of nerves with neuromeres is established almost at the same time that the inner surface of the hindbrain neuromeres becomes concave, it might be thought that this change is due to the mechanical effect of nerve fibres. That such is not the case seems clear, however, because no nerve fibres come into relation with the outer convexity of encephalomere VI. The hindbrain neuromeres, from their early appearance onwards until they disappear, are local differentiations of the walls of the medulla, and as such are not, I believe, to be satisfactorily explained on simple mechanical grounds. On the other hand, I hold that they do possess certain characteristics which admit of a mechanical explanation. This seems to be supported by evidence from two sources. In the first place, a fixing agent which causes a contraction of the tissues of the embryo intensifies the constrictions between the neuromeres. By this means the radial arrangement of cells

¹ This is true also in swine and chick embryos; but I do not find in *Amblystoma* as good evidence that the neuromeres are local thickenings of the neural wall.

and nuclei is still more sharply emphasized. I think we may safely assume that this effect is the same as that resulting from a shoving of the neural tube due to rapid growth in a confined space. Figure 28 (Plate 5) shows a frontal section of a preparation of a shark embryo, nearly 10 mm. long. The specimen was fixed in the mixture of picrosulphuric and chromic acids, and then transferred directly to 50 per cent alcohol. Inadequate fixation and immediate transference to a fluid of very different osmotic power resulted in a strong contraction of the embryo, particularly emphasized in the wall of the neural tube. (In the figure the constrictions appear exaggerated, since only the regions of the nuclei are shaded.) Moreover, a comparison of embryos of different Vertebrates gives evidence, as it seems to me, that the bending of the neural tube results in the intensification of the characteristics of neuromeres. I have studied in frontal section embryos of *Petromyzon*, *Gadus*, *Amblystoma*, *S. acanthias*, chick, and swine. The radial arrangement of cells is more pronounced in those forms which have a stronger flexure, and in which, therefore, we may safely assume that there is a greater shoving of the neural tube, due to rapid growth in a confined space. These characteristics are considerably more pronounced in *Sauropsida* than in *S. acanthias*, in which the flexure of the neural tube is, however, considerable. This explanation tends to remove the doubt as to the phylogenetic value of such structures as the neuromeres which naturally arises when these are shown to be structures slightly if at all visible in the lowest Vertebrates (*Amphioxus* and *Cyclostomes*), while well marked in the highest. I believe that the presence of yolk makes the conditions in both *Petromyzon* and *Amblystoma* less primitive than in *Squalus*, chick, and swine.

In *Gadus* and *Amblystoma* the radial arrangement of cells and nuclei is even less pronounced than in *S. acanthias*, and this seems to be correlated with the fact that the flexure of the neural tube in the former is less marked than in the latter. It must be admitted, however, that the presence of much yolk in the cells of the neural tube of *Amblystoma* (Plate 5, Fig. 35), in which no sign of encephalomere IV is present, may be concerned in producing the different condition of this form, in which the outpocketing of the neural tube takes place in the region of the proliferations of the ganglionic Anlagen only. Broman ('95, p. 186) has given proof, satisfactory as it seems to me, that the nuclear and cellular characteristics of the neuromeres of the human embryo may be explained partly on mechanical grounds. Embryologists are agreed that the flexures of the neural tube may be accounted for by the rapid growth of the

tube in a confined space. Such growth would clearly result in a shoving of the neural tube, and also in a flexure in weaker portions, as in the regions between local thickenings, like the hindbrain neuromeres. The crowding of the cells in the regions of constriction between neuromeres may be accounted for in the same way. I therefore conclude that *some* of the structural characteristics of neuromeres may be intensified by the bending or shoving of the neural tube during its growth.

The conditions presented in *Amblystoma* (Plate 5, Fig. 35) led me to believe at one time that the neuromeres might be related to the proliferation of the cells of the ganglionic Anlage. In this animal the neural tube is evaginated in the regions of the proliferation of cells for the ganglionic Anlagen of nerves V, VII, IX, and X, while in the region where no neural-crest cells are proliferated — the region corresponding to the position of encephalomere IV (in other forms) — no neuromere appears.¹ In *S. acanthias* we have seen (page 215) that from two of the hindbrain neuromeres, viz. V and VI, are proliferated the cells of two distinct nerve Anlagen. But since no nerve Anlage is proliferated from encephalomere IV, although this is as well marked as other encephalomeres, I was compelled to abandon the hypothesis, to which the study of *Amblystoma* had inclined me. *The fact that particular nerve Anlagen are proliferated from particular encephalomeres may, however, be a clue to the primitive mutual relationships of these nerves and of the encephalomeres to each other.* The fact that the local thickenings are confined to that region of the neural tube from which the great nerves of the head — V, VI, VII, IX, and X — arise, must also give us some clue as to their significance. Such local thickenings are seen neither in the region anterior, nor in that posterior to the medulla, but they are not limited by the ear capsule posteriorly, and the anterior boundary of them does not coincide with the anterior boundary of the primary hindbrain vesicle. It is to their nerve relations, then, that an investigator must first turn his attention. We have seen that in the development of the neural crest some of the cells of the trigeminus are proliferated from encephalomere III; that few cells are proliferated from encephalomere IV; that from encephalomere V come the cells of the acustico-facialis, from encephalomere VI the cells of the glossopharyngeus, and from encephalomere VII the cells of the Urvagus. The clearly marked relations of the Anlagen of the two suc-

¹ The migration of cells from certain regions of the neural tube would certainly weaken these regions, and the tube would in consequence, if subjected to a longitudinal pressure, or to distention by growth, tend to bend or distend most readily in such places.

cessive nerves, the facialis and the glossopharyngeus, to two successive encephalomeres (V and VI), seems to me to be a very important fact.¹ The cells of the glossopharyngeus are crowded back by the ear capsule, but the fact that in their ventral course they are directed anteriorly into the third visceral arch goes to prove that their posterior position is not their primitive one. Almost as clear is the relation of the cells proliferated from encephalomere VII to the second branchial (4th visceral) arch. From these facts I was led to think that the primitive relations of the hindbrain neuromeres were with the visceral arches. The fact that the hindbrain neuromeres are local thickenings of the lateral walls of the medulla also leads to the opinion that they are segmental groupings of the "Kerne"² of the nerves of the visceral arches. With this hypothesis in mind, I have examined the evidence in *S. acanthias*, as well as in other forms, in order to see if the facts support it. The more primitive relations would be expected to occur in *S. acanthias*. From encephalomere III are proliferated neural-crest cells which enter the mandibular arch; later this encephalomere becomes related with the motor root which innervates the muscles of this (mandibular) arch. Its relations, then, are clearly with the first visceral arch, and we may therefore assume that its local thickening contains, at least in part, the "nucleus" of the trigeminus.

The evidence obtained from the study of the relations of encephalomere IV seems at first sight strongly against the hypothesis. Few cells are proliferated from this neuromere. Late in its development the fibres of the sensor root of the trigeminus connect with its convexity. It forms a marked exception in its nerve relations to the other hindbrain neuromeres. Were it not that other facts are found which serve to bring this apparent exception into harmony with the hypothesis, the adverse evidence it presents would seem an insurmountable obstacle to the acceptance of my view. Neural-crest cells which pass into the second visceral (the hyoid) arch are proliferated from hindbrain neuromere V, and the motor fibres in relation with this neuromere innervate the muscles of this arch. From hindbrain neuromere VI are proliferated the neural-crest cells which pass into the third visceral (1st branchial) arch, and the motor fibres of the glossopharyngeus, of which these cells form the ganglionic Anlage, innervate its musculature. The place of origin of the fibres of the glossopharyngeus is crowded backward, evidently by

¹ Hoffmann ('94) has spoken of the paired segmental outpocketings of the neural tube of this region.

² That is, they may be localizations of the motor "Kerne" and of the sensor "Endkerne" of the nerves primitively related to them.

the growth of the ear capsule. The place of origin of the roots of this nerve are variable. In swine and chick, for example, they have their origin from encephalomere VII, while in *S. acanthias* they arise behind this encephalomere. This is correlated with the fact that the ear capsule in *S. acanthias* is crowded backward into the region opposite encephalomere VII, whereas in the swine and chick the ear capsule continues to lie opposite encephalomere VI until long after the nerve assumes fibrillar connections with the neural tube. We may thus explain the variation in the position of the roots of this nerve, and still believe from the evidence that their primitive relations were with encephalomere VI.

Again, the cells proliferated from encephalomere VII are those which pass into the fourth visceral (2d branchial) arch, and form the Anlage of the Urvagus, whose motor fibres innervate the musculature of that arch. The Urvagus assumes fibrillar connections with the neural tube at a point behind the origin of the glossopharyngeus, and the cause of this change of relation may safely be assumed to be the same as in the case of that nerve. We have good evidence, then, that the primitive relationships of four of the hindbrain neuromeres were with the first four visceral arches. This relationship consists chiefly, but not wholly, in the fact that from these four neuromeres are proliferated cells which enter these arches and there form, in part at least,¹ the ganglionic Anlagen of the nerves related with them. The origin of these cells from the neural crest would naturally lead us to infer that in dealing with them as nerve Anlagen we are not dealing with motor nerves. We are, however, really dealing with the Anlagen of nerves which later become mixed. But in later stages, when the nerve roots are established, the roots of only two of the nerves in question, viz. V and VII, have their exit from the encephalomes from which their ganglionic Anlagen arose. Have we a right, then, to assume that the exits of the roots of the other two nerves, IX and X (Urvagus), have been pushed back from the position which may be assumed, on the evidence of the relations of their ganglionic Anlagen, to have been the primitive one? I believe that we have, because, as we have seen from the examination of the relations of the roots of these two nerves, these roots lie as close to the point of origin of their ganglionic Anlagen as the ear capsule will permit. In a

¹ Part of the neural-crest cells surrounds the mesoderm of the visceral arches, and very probably gives rise to some of the connective tissue of the arches. (See Plate 6, Fig. 40, *cl. crs. n.*) Whether or not they later form the cartilages of the arches, as they are said to do in *Necturus* (Platt, '94, '97), is a question which requires more careful and prolonged study than I have been able to give.

form like *S. acanthias*, where the ear capsule shifts backward, the exit of the root of the glossopharyngeus lies behind encephalomere VII, whereas in such forms as the chick and swine, where the ear capsule does not similarly shift backward, the exit of its root is from the expansion of encephalomere VII. In all Vertebrates, the roots of the glossopharyngeus and the Urvagus lie close to each other, but in *S. acanthias*, where there is a greater amount of posterior displacement than in any other Vertebrate that I have studied, these roots are more crowded together than in other forms. These facts seem to me to warrant the conclusion that the roots of the glossopharyngeus and the Urvagus primitively made their exit from those encephalomeres which give rise to their ganglionic Anlagen. And we may likewise assume that the local thickenings of these encephalomeres have their significance in this primitive relation, i. e. they contained the "Kerne" of these roots. I am able to find no facts which render this assumption untenable.

On the other hand, encephalomere IV never has nervous connection with a visceral arch. From it few neural-crest cells are proliferated, and in consequence it never forms the ganglionic Anlage of a nerve, nor does it ever in ontogeny have a motor nerve in connection with it. Since the other four encephalomeres are related to visceral arches, I incline to think that this encephalomere was once related to a visceral arch of its own. Otherwise, so far as I can see, its existence is inexplicable. In this condition, then, I find additional evidence of a lost visceral arch, which van Wijhe ('82), Miss Platt ('91*), and Hoffmann ('94) believe once existed in the region of this neuromere. These investigators have found a want of exact correspondence between the somites and the visceral arches in the region of the spiracular cleft. Van Wijhe was led to believe that the *hyoid* (2d visceral) arch is double, — i. e. represents two arches, the fusion of which has resulted in the obliteration of the visceral cleft between them, — while Miss Platt and Hoffmann have held that the *mandibular* arch is double, and that an anterior gill cleft has disappeared. The disappearance of a visceral cleft is rendered plausible, if we assume that such a loss would greatly strengthen the mandibular arch when it came to function as a lower jaw. The evidence from a study of mesomerism and neuromerism therefore seems mutually confirmatory.

If encephalomere IV was related to a lost visceral arch, it follows that the lost arch must have been situated posterior to the mandibular (1st visceral) arch, for the musculature of this arch is innervated from encephalomere III. It also follows, because of the relation of the nerve

of encephalomere V (facialis) to the present spiracular cleft, that this was once the second visceral cleft instead of the first (disregarding for the present the possibility that the mouth represents a pair of gill clefts), as it now is. It seems entirely possible that the outpocketing of the present first visceral (hyo-mandibular) cleft was originally a double one,¹ and that the fusion of these two outpocketings resulted in the loss of the visceral arch which once separated them, and therefore in the loss of the nerve primitively related to that arch. Moreover, between the second head somite of van Wijhe, which extends into the mandibular arch, and the fourth somite, which is widely connected with the mesoderm of the hyoid arch, there lies the third head somite, in correlation with which there is no intermediate visceral arch. This somite (the 3d) lies opposite the posterior constriction of neuromere IV, and speaks plainly for the previous existence of a lost head segment, for which neuromere IV may once have furnished the nerve centre. Did such an arch exist, each of van Wijhe's somites from the second to the sixth, and each of the encephalomes from III to VII would correspond with a visceral arch.

I give a brief summary of the line of reasoning which leads me to believe that the significance of the hindbrain neuromeres lies in their primitive relationship to the visceral arches. In the young embryos of *S. acanthias* two facts, both so far as I know new, present themselves. In the first place, the hindbrain neuromeres, five in number, are found to be successive similar thickenings of the lateral zones of the medulla. Secondly, from four of them, viz. III, V, VI, and VII, are proliferated the ganglionic cells of the four cranial nerves which innervate the first four visceral arches, viz. the trigeminus, the facialis, the glossopharyngeus, and the Urvagus. A clue to the significance of the local thickenings of the neural wall in the tract of the encephalomes is given in the fact that from those two encephalomes which (in other Vertebrates as well as in *S. acanthias*) most closely retain these primitive nerve relationships, viz. III and V, emerge the fibres which innervate the visceral arches (primitively) related to them. The thickenings are the first expression of the "Kerne" (nuclei) of the nervous centres related to the visceral arches, and possibly also, primitively, of those related to the somites.

¹ Kupffer ('93) finds in *Acipenser* embryos an entodermal outpocketing or pouch, which soon disappears, just anterior to the hyomandibular pouch. The position of this pouch would identify it with the cleft whose former existence seems probable on the evidence given above. Houssay ('91) also recognizes in *Amblystoma* a visceral cleft between the oral and the hyomandibular.

A study of neural segments anterior and posterior to the medulla has led me to the conclusion that the *local thickening* is a more essential characteristic of a hindbrain neuromere than the commonly accepted criteria, viz. the radial arrangement of cells in the neuromere, and the crowding of them in the regions of constriction between neuromeres, both of which may be the result of mechanical influences.

The shifting of the point of exit of the roots primitively related to encephalomes VI and VII may easily be explained as the result of the crowding caused by the ear capsule. Since four hindbrain neuromeres are clearly related to four visceral arches, we should expect the remaining one, encephalome IV, to have been primitively related to a visceral arch. That such an arch has been present in the region of this neuromere during phylogeny, has been made probable by the studies of van Wijhe ('82), Miss Platt ('91), and Hoffmann ('94). The evidences from the study of neuromerism and mesomerism are mutually confirmatory, and to the effect that *a visceral arch has been lost in the region of encephalome IV and van Wijhe's third somite*. Having established an exact numerical correspondence between encephalomes and somites (head cavities), and a probable primitive correspondence of hindbrain encephalomes with visceral arches, I conclude that *in the head region there existed primitively a correspondence between neuromerism, mesomerism, and branchiomerism*. Since this correspondence is not to-day exact in *Squalus* or in any other known Vertebrate, it seems necessary to discuss somewhat in detail the constituent parts of the anterior or more highly modified metameres, and to inquire what may be inferred as to their previous conditions. The table on the opposite page, although in part theoretical, will help to make the discussion clearer.

I have in this table included neuromeres as far posteriorly as the eleventh. Accepting Hoffmann's ('94) conclusion that vertebral arches as far back as that which corresponds with van Wijhe's tenth somite fuse into the cranium of the adult *Squalus*,¹ it would follow that neuromeres I to XI would be included in the cranium. The variability in the number of segments added to the occipital region of the cranium in different Selachii and Ichthyopsida (Fürbringer, Sewertzoff) makes the exact number in *Squalus* a matter of no great morphological importance.

We see that the cephalic segments are highly modified segments altered by reduction or enlargement (possibly even by substitution and change of relation, as, for example, in the case of the vagus segments) of

¹ Recently confirmed by Sewertzoff ('98).

TABLE III.—NEUBOMERES I TO XI IN SQUALUS, AND THEIR RELATIONS TO NERVES, SOMITES, AND VISCERAL ARCHES.

CEPHALIC METAMERES.										
NEUBOMERES										
	SOMITES . . .									
Nerves (dorsal)										
	Nerves (ventral)									
Visceral clefts										
	Visceral arches									
I	II	III	IV	V	VI	VII	VIII	IX	X	XI
1	1	2	8	4	5	6	7	8	9	
2	1	2	8	4	5	6	7	8	9	
3	1	2	8	4	5	6	7	8	9	
4	1	2	8	4	5	6	7	8	9	
5	1	2	8	4	5	6	7	8	9	
6	1	2	8	4	5	6	7	8	9	
7	1	2	8	4	5	6	7	8	9	
8	1	2	8	4	5	6	7	8	9	
9	1	2	8	4	5	6	7	8	9	
10	1	2	8	4	5	6	7	8	9	
11	1	2	8	4	5	6	7	8	9	
12	1	2	8	4	5	6	7	8	9	
13	1	2	8	4	5	6	7	8	9	
14	1	2	8	4	5	6	7	8	9	
15	1	2	8	4	5	6	7	8	9	
16	1	2	8	4	5	6	7	8	9	
17	1	2	8	4	5	6	7	8	9	
18	1	2	8	4	5	6	7	8	9	
19	1	2	8	4	5	6	7	8	9	
20	1	2	8	4	5	6	7	8	9	
21	1	2	8	4	5	6	7	8	9	
22	1	2	8	4	5	6	7	8	9	
23	1	2	8	4	5	6	7	8	9	
24	1	2	8	4	5	6	7	8	9	
25	1	2	8	4	5	6	7	8	9	
26	1	2	8	4	5	6	7	8	9	
27	1	2	8	4	5	6	7	8	9	
28	1	2	8	4	5	6	7	8	9	
29	1	2	8	4	5	6	7	8	9	
30	1	2	8	4	5	6	7	8	9	
31	1	2	8	4	5	6	7	8	9	
32	1	2	8	4	5	6	7	8	9	
33	1	2	8	4	5	6	7	8	9	
34	1	2	8	4	5	6	7	8	9	
35	1	2	8	4	5	6	7	8	9	
36	1	2	8	4	5	6	7	8	9	
37	1	2	8	4	5	6	7	8	9	
38	1	2	8	4	5	6	7	8	9	
39	1	2	8	4	5	6	7	8	9	
40	1	2	8	4	5	6	7	8	9	
41	1	2	8	4	5	6	7	8	9	
42	1	2	8	4	5	6	7	8	9	
43	1	2	8	4	5	6	7	8	9	
44	1	2	8	4	5	6	7	8	9	
45	1	2	8	4	5	6	7	8	9	
46	1	2	8	4	5	6	7	8	9	
47	1	2	8	4	5	6	7	8	9	
48	1	2	8	4	5	6	7	8	9	
49	1	2	8	4	5	6	7	8	9	
50	1	2	8	4	5	6	7	8	9	
51	1	2	8	4	5	6	7	8	9	
52	1	2	8	4	5	6	7	8	9	
53	1	2	8	4	5	6	7	8	9	
54	1	2	8	4	5	6	7	8	9	
55	1	2	8	4	5	6	7	8	9	
56	1	2	8	4	5	6	7	8	9	
57	1	2	8	4	5	6	7	8	9	
58	1	2	8	4	5	6	7	8	9	
59	1	2	8	4	5	6	7	8	9	
60	1	2	8	4	5	6	7	8	9	
61	1	2	8	4	5	6	7	8	9	
62	1	2	8	4	5	6	7	8	9	
63	1	2	8	4	5	6	7	8	9	
64	1	2	8	4	5	6	7	8	9	
65	1	2	8	4	5	6	7	8	9	
66	1	2	8	4	5	6	7	8	9	
67	1	2	8	4	5	6	7	8	9	
68	1	2	8	4	5	6	7	8	9	
69	1	2	8	4	5	6	7	8	9	
70	1	2	8	4	5	6	7	8	9	
71	1	2	8	4	5	6	7	8	9	
72	1	2	8	4	5	6	7	8	9	
73	1	2	8	4	5	6	7	8	9	
74	1	2	8	4	5	6	7	8	9	
75	1	2	8	4	5	6	7	8	9	
76	1	2	8	4	5	6	7	8	9	
77	1	2	8	4	5	6	7	8	9	
78	1	2	8	4	5	6	7	8	9	
79	1	2	8	4	5	6	7	8	9	
80	1	2	8	4	5	6	7	8	9	
81	1	2	8	4	5	6	7	8	9	
82	1	2	8	4	5	6	7	8	9	
83	1	2	8	4	5	6	7	8	9	
84	1	2	8	4	5	6	7	8	9	
85	1	2	8	4	5	6	7	8	9	
86	1	2	8	4	5	6	7	8	9	
87	1	2	8	4	5	6	7	8	9	
88	1	2	8	4	5	6	7	8	9	
89	1	2	8	4	5	6	7	8	9	
90	1	2	8	4	5	6	7	8	9	
91	1	2	8	4	5	6	7	8	9	
92	1	2	8	4	5	6	7	8	9	
93	1	2	8	4	5	6	7	8	9	
94	1	2	8	4	5	6	7	8	9	
95	1	2	8	4	5	6	7	8	9	
96	1	2	8	4	5	6	7	8	9	
97	1	2	8	4	5	6	7	8	9	
98	1	2	8	4	5	6	7	8	9	
99	1	2	8	4	5	6	7	8	9	
100	1	2	8	4	5	6	7	8	9	

1 Possibly also representing a visceral pouch.
2 Fuses with the dorsal ganglion of X in later stages.
3 Represented by ganglia which probably disappear in development.
4 Form the first three roots of the embryonic hypoglossus nerve.
5 Found in Hexanchus, Heptanchus, and Chlamydoselachus.
6 Possibly represented in the two labial cartilages.
7 Roman numerals bracketed indicate the theoretical nerve relationships.

parts of the original segments. Fortunately, however, with the knowledge that neuromeres and mesomeres correspond numerically, we are able to see that the majority of changes which have occurred are correlated ones, and therefore capable of explanation. We furthermore see that the greatest changes have taken place in the more anterior metameres, chiefly and primarily by the loss of the ventral parts of these metameres. Since the more posterior of the cephalic segments have indubitable metamerie value, I shall discuss in detail only those anterior ones (viz I to VII) concerning which there is most disagreement among morphologists, beginning with the consideration of the seventh, whose relations are least modified.

VIII. Primitive Relations of Cephalic Segments.

a. •RELATIONS OF ENCEPHALOMERE VII.

Opposite the posterior constriction of this encephalomere in very early stages lies van Wijhe's 6th somite, which develops embryonic muscle fibres and is universally considered a true somite. I therefore regard this as the mesomere corresponding with encephalomere VII, whose neural-crest cells first meet the mesoderm opposite the anterior constriction of this somite (Plate 3, Fig. 13). These cells form the Anlage of the anterior branch of the vagus (Urvagus), and I assume that the primitive relations of this nerve were with the myoseptum between the 5th and 6th somites. The intermediate position of the Urvagus with respect to the myotomes and its ontogenetic union with spinal ganglia in some Vertebrates serves to show that there is no fundamental difference in this respect between cranial and spinal nerves. For reasons which will be stated in connection with the study of the relations of encephalomere IV, I regard the abducens (Plate 4, Fig. 21), whose fibres have their exit from the ventral horn of encephalomere VII, as representing in part the ventral nerve of this segment. Furthermore, I assume that the mesoderm of the 6th somite was primitively connected with the mesoderm of the 4th visceral arch (Plate 3, Fig. 16); because that somite in *Ammocoetes* which I regard as its exact homologue, viz. the 2d post-otic somite, is certainly in early stages thus connected. Consequently the present 3d visceral cleft bounds ventrally the visceral (splanchnic) portion of this segment.

b. RELATIONS OF ENCEPHALOMERE VI.

The present structure and relations of the component parts of what I regard as the primitive sixth cephalic segment have been considerably changed cœnogenetically by the development of the otic capsule. Arising from what in all probability was primitively a sensor organ of the dorsal lateral line (Ayers), the great enlargement and subsequent invagination of this capsule bring about ontogenetically the degeneration of the musculature of the 5th somite, whose cells, after assuming the elongated spindle form of embryonic muscle cells, are transformed in early stages into loose mesenchyma. In *Ammocetes*, however, only the median portion of the 1st post-otic somite disappears during ontogeny, while the lateral portion forms the most anterior segment of the lateral body musculature (muscle. *lateralis capitis anterior*, von Kupffer). Furthermore, in *Squalus* the development of the otic capsule causes a shifting backward of the point of exit of the fibres of the glossopharyngeus, whose ganglion cells were proliferated from encephalomere VI; moreover, the fibres of this nerve may be traced in the neural tube as far forward as encephalomere VI, in which, it is my opinion, their nuclei lie. The growing ganglionic Anlage of this nerve meets the mesoderm between the 4th and 5th somites (Fig. 13), and I assume that it was primitively related, as are the dorsal nerves of *Amphioxus*, to a myoseptum, i. e. the one primitively between somites 4 and 5. The sensor fibres of this nerve innervate the skin of the present 2d visceral cleft (Fig. 14), which was, I assume, primitively inter-somitic in position and situated ventral to the myoseptum between the 4th and 5th somites. Its motor fibres innervate the splanchnic musculature of the present 3d visceral arch, probably a primitive relation. The abducens nerve, I believe, represents the primitive ventral nerve of this metamere.

c. RELATIONS OF ENCEPHALOMERE V.

The fourth somite, the one corresponding to the fifth cephalic segment, is the most rudimentary of all the cephalic somites. The phylogenetic loss of its musculature and the ontogenetic dissolution of its cells into a loose mesenchyma may be explained as due to the same cause as that operative in the case of the 5th somite, the development of the otic capsule. The dorsal nerve of this segment, the *facialis*, is inter-somitic in position, occupying the constriction dividing the 3d and 4th somites (Figs. 11-17), and its motor fibres innervate the (splanchnic) musculature of the corresponding (2d visceral or hyoid) arch. Correlated with

the loss of the somatic musculature of this segment, a somatic (ventral) nerve is wanting, and as in the case of the 6th segment I assume that this is to-day represented by the abducens. Since the sensor fibres of the facialis innervate the skin of the hyomandibular (1st visceral) cleft, this cleft may be believed to have been primitively situated ventral to the constriction between the 3d and 4th somites. I find no evidence to support the view that the hyoid arch represents two splanchnic segments.

d. RELATIONS OF ENCEPHALOMERE IV.

As has already been stated, there is no ganglionic nerve Anlage proliferated from encephalomere IV, and although the fibres of the major root of the trigeminus have their exit in early stages from its outer convexity, the probability is that such relation of nerve V is secondary, and therefore not of phylogenetic significance. I hold that this encephalomere, by virtue of its local thickening, affords evidence of a lost visceral arch, the loss of which would naturally be correlated with the loss of the dorsal nerve. Since, however, the disappearance of the splanchnic portion of this segment may have been due simply to a union with the corresponding portion of the anterior (mandibular) segment, it is also possible that the dorsal nerve has fused with the nerve of the anterior segment, the trigeminus. This conclusion seems indeed supported by the evidence that at least some of the fibres of the trigeminus roots have their nucleus in the lateral horn of this (4th) encephalomere.

In a scheme of primitive segmental relations such as I am at present advocating, there is likewise difficulty in explaining the fact that the somite (van Wijhe's 3d) which I assume to correspond with encephalomere IV is innervated by the abducens, whose fibres make their exit from encephalomere VII. The evidence which leads me to conclude that the abducens to-day represents the primitive ventral nerve of this encephalomere, as well as those of encephalomes V, VI, and VII, has been partly given in connection with the study of its development; it may be summarized as follows. (1) Its roots are many (4-6 in various *Selachii*) and more widely separated than those of any other nerve. (2) Not only do abducens fibres innervate pre-otic musculature (musculus rectus posterior), but fibres from this nerve may also be traced for a considerable distance in the mesoderm of the embryo posterior to encephalomere VII (Fig. 20). (3) The variability as to the place where its fibres emerge, as shown by comparative embryological evidence, appears to indicate that its relations are not limited to any single encephalomere. (4) Its nucleus in the ventral horn of the neural tube is greatly elongated.

(5) In *Torpedo* it innervates musculature (musco. rectus posterior) derived from *two* somites, viz. van Wijhe's third and *fourth* (Sewertzoff, '98). I am not able, however, to offer direct evidence that the nerve has part of its nucleus in encephalomere IV. I am therefore not able to exclude the possibility that the ventral root of a post-otic somite has been substituted for the pre-otic ventral nerve which once innervated somite 3. That such a substitution of the fibres of a ventral nerve of one segment for those of another may take place ontogenetically, I have the following evidence. I find that in a *Squalus* embryo of 50 mm. the ventral nerve of van Wijhe's 7th somite has become very rudimentary, while fibres from the ventral nerve of the 8th somite extend to the musculature derived from the 7th somite, which in this stage forms the most anterior segment of the lateral musculature. Now, if the ventral root of the 7th somite atrophies before the adult stage is reached, and if the musculature derived from this somite remains the first segment of the lateral trunk musculature of the adult, as has been stated by van Wijhe ('82) and Hoffmann ('94), the conclusion seems unavoidable that we have to do here with a substitution of a posterior nerve for one farther anterior. Moreover, in *Petromyzon* we have evidence that the first five post-otic myotomes of the lateral trunk musculature are innervated by the ventral nerves of the last two of the corresponding somites, i. e. the 4th and 5th post-otic, which in my opinion are homologous with the 4th and 5th post-otic somites of *Squalus* (van Wijhe's 8th and 9th). Here also the conclusion seems to me to be warranted that there has been a phylogenetic, if not an ontogenetic, substitution of the nerves of posterior segments for those of more anterior segments.¹ We may therefore infer, with a considerable degree of probability, that a similar substitution of a post-otic nerve for a pre-otic one may have occurred phylogenetically in the case of the abducens. Such evidence, however, seems to render unwarrantable the assumption of a primary and inseparable connection of motor nerve and muscle. Furthermore, the evidence that the motor nerves develop as axis-cylinder processes of medullary cells given by His ('89) for spinal nerves, and by myself in this

¹ See Neal ('97, Figure 2, p. 446) for evidence that the fibres of a post-otic ventral nerve (hypoglossus auctorum) extend into the pre-otic region with the muscle they innervate. It would seem a very easy matter for such fibres to come into nervous connection phylogenetically with the eye muscles, and especially the posterior of these, with which in *Petromyzon* they are very closely connected. Hatschek ('92) stated that the musco. rectus posterior becomes connected with the anterior of the post-otic myotomes. See evidence given by M. Fürbringer ('97) and Neal ('97) upon this question.

paper for cranial ventral nerves in Selachii, leads to the same conclusion. The visceral cleft which defined anteriorly the splanchnic part of the fourth segment is not ontogenetically evident in *Squalus*. Kupffer ('93) has possibly seen evidence of a rudimentary cleft between the mouth and the hyomandibular cleft of *Acipenser*. And possibly this cleft may be represented in the "Pseudobranchialrinne" of *Amphioxus*.

e. RELATIONS OF ENCEPHALOMERE III.

As in the case of the four posterior hindbrain segments, the study of the development of the nerves connected with encephalomere III (Hinterhirn) gives the clue to the primitive relations of this primary vesicle. The neural-crest cells proliferated from it pass ventrally into the mandibular arch. From a part of these a large ganglion is formed (the Gasserian), through which pass the motor fibres, whose nucleus is, at least in part, in encephalomere III, to innervate the musculature of the first visceral (mandibular) arch. We have thus the splanchnic elements of a cranial segment. In the Table of Nerve Relations (p. 253) the trochlearis has been given as the ventral (somatic) nerve of this segment. The evidence in favor of this view has already been stated, and consists in the facts that it innervates musculature derived from dorsal (somatic) mesoderm, that its fibres develop as processes of neuroblasts in the neural tube, and that its histological relations and structure in the adult show it to be a purely motor nerve with motor nucleus in the ventral horn of encephalomere III. I regard the mouth as representing the fused visceral clefts which bounded anteriorly the splanchnic portion of this segment. We have thus all the essential elements of a head metamere.

f. RELATIONS OF ENCEPHALOMERE II.

From the simple dorsal expansion of encephalomere II are proliferated cells which pass ventrally and fuse with the skin to form the mesocephalic ganglion¹ lateral to the 1st somite (Figs. 17 to 20). Although this ganglion never becomes connected with the midbrain (encephalomere II), since its fibres enter the brain through the r. ophthalmicus profundus V, it must in my opinion be regarded as a segmental ganglion comparable with those of the following cranial nerves; the ophthalmicus profundus must likewise be considered as a dorsal nerve homodynamic with the succeeding cranial nerves. Its want of motor fibres may be explained as resulting from phylogenetic loss, since in

¹ This ganglion is homologous with the first trigeminal ganglion of *Cyclostomes*.

Myxinoids this nerve possesses motor fibres (J. Müller, P. Fürbringer, Price), and its segmental value as a dorsal nerve seems thereby established. The fact that the fibres of the ophth. profundus V enter the brain at a point posterior to encephalomere III, instead of anterior to it, as they should in order to conform to my scheme of segmental relations, appears to me no serious objection. That they enter the brain at a point posterior to that at which the motor fibres innervating the mandibular musculature enter, and in consequence cross these fibres in the mesocephalic ganglion, is to be explained by the tendency, especially of the sensor cranial nerves, to enter the brain as near the otic capsule as possible (see Ahlborn, '84*), and by the more conservative relations of the motor fibres (roots) generally.

In my preliminary paper I placed tentatively the so called "thalamic" nerve as the possible dorsal nerve of encephalomere II. Now, however, I question the correctness of this opinion. We certainly need something more than a strand of neural-crest cells which persist for some time in a region of constriction between encephalomeses, but *which never assume fibrillar relation with the neural tube*, to warrant us in assuming that we have to do with a *nerve*.¹

The development and relations of van Wijhe's first somite and of the oculomotorius leave no doubt that in them we have the somatic elements of a metamere. Probably no ventral or splanchnic portion of the mesoderm of this segment exists, consequently the r. ophthalmicus profundus possesses no splanchnic fibres.² In my opinion it is doubtful if the hypophysis may be regarded as evidence of an ancestral visceral cleft between segments I and II.

However, I hold that the structural comparability of encephalomere II with hindbrain encephalomeses, together with the evidence of its relation with a segmental ganglion, and of its connection with somatic musculature by means of a ventral motor nerve, strongly favors the view that it is serially homologous with hindbrain encephalomeses.

g. RELATIONS OF ENCEPHALOMERE I.

That which I regard as the first cephalic segment of Craniota consists of an encephalomere (primary forebrain) which has been shown to be

¹ Kupffer excels Miss Platt in discovering "rudimentary" nerves, but until we have a better criterion for a nerve than a cellular strand there is no reason why the number of "rudimentary" nerves should not be much larger than it is at present recognized to be.

² Possibly the skeletogenous element of the ventral portion of this segment is to be found in the "maxillar Lippenknorpel" of Gegenbaur.

morphologically comparable with the hindbrain encephalomeres. It is in connection with a sensor nerve, the olfactory, which appears comparable with the sensor portion of a dorsal segmental nerve in so far as it is composed of bipolar ganglion cells which send their fibres into the brain and, in my opinion, are in part derived from the neural crest. My observations upon this point, however, are as yet incomplete. The want of motor fibres in the dorsal nerve of this segment is correlated with the want of splanchnic musculature.¹ That structure which I, in agreement with Miss Platt ('91) and Hoffmann ('94 and '96), regard as a rudimentary somite (compare Plate 3, Figs. 16, 17, *cav. a.*), — since it resembles the following somites and gives evidence of producing rudimentary muscle cells, — represents the somatic portion of this segment. In correlation with the want of fully developed musculature, no ventral somatic nerve is present. Van Wijhe ('86*, p. 680) wrote: "Wenn der Olfactorius ein segmentaler Nerv wäre, müsste man bei demselben das ursprüngliche Vorhandensein eines Somiten und einer zugehörigen ventralen Nervenwurzel annehmen. Von beiden ist keine Spur vorhanden." So far as the somite is concerned, it appears that in the "anterior somite"² we now have the requisite evidence. The lateness of the differentiation of the "premaxillar Lippenknorpel" makes it seem at most only remotely possible that it may be regarded as the ventral skeletogenous element of this segment.

A. COMPARISON WITH THE SEGMENTATION OF AMPHIOXUS.

A comparison of the segmentation of *Squalus* as shown in Table III. (p. 253) with that of *Amphioxus* is of interest, inasmuch as it appears to favor important conclusions reached by the study of *Squalus* alone. However, before stating my own conclusions concerning the primitive metamerism of *Amphioxus* and the homologies of its segments with those of *Squalus*, it will be well to review the conclusions of previous investigators.

A comparison of their results may be made in the form of a table on the opposite page (after M. Fürbringer, '97, p. 643, slightly modified).

While Hatschek ('92), Willey ('94), and M. Fürbringer ('97) homologize the mouth of *Amphioxus* with that of Tunicates and Craniota, but

¹ Likewise in *Amphioxus* the anterior dorsal nerve is generally believed to be purely sensor in function.

² Van Wijhe ('82) saw the "anterior somite" in *Galeus*, but unfortunately possessed only one embryo; he was therefore unable to express an opinion concerning its segmental value, based on a knowledge of its development and differentiation.

TABLE IV.

	FATE OF		HATSCHEK, '92.		VAN WIJNE, '93.		WILLET, '94.
1	Unpaired mouth.		Single persisting mouth, the homologue of the median unpaired mouth of Tunicates and higher Vertebrates.		Primary mouth (Autostoma) pushed toward the left and modified to form the pre-oral pit (Räderorgan).		Single persisting mouth, the homologue of the mouth of Tunicates and higher Vertebrates.
2	1st visceral pouch (vorderes Entodermäckchen) of Hatschek.	Right.			Perhaps the homologue of the 1st head cavities (1st somites) of Selachii.		Probable homologue of the right 1st (premandibular) head cavity of Craniota.
		Left.	Pre-oral pit (Räderorgan; Sinnesorgan).		Pre-oral pit; also primary mouth (Autostoma).		Pre-oral pit, probable homologue of the left 1st (premandibular) head cavity of Craniota.
3	2d visceral pouch of Hatschek (1st visceral cleft of van Wijne and Willet).	Right.	Right pseudo-branchial groove.		Club-shaped gland.		Club-shaped gland.
		Left.	Left pseudo-branchial groove.		Secondary permanent mouth (Tremostoma). (Spiracular cleft of Selachii).		1st (abortive) primary gill slit.
4	3d visceral pouch of Hatschek (2d visceral cleft of van Wijne and Willet).	Right.	1st permanent right visceral cleft.		Lost.		2d (1st permanent) secondary or right gill slit.
		Left.	1st permanent left visceral cleft.		Lost.		2d (1st permanent) primary gill slit.
5	4th visceral cleft of Hatschek (3d visceral cleft of van Wijne and Willet).	Right.	2d permanent right visceral cleft.		1st permanent right visceral cleft.		3d (2d permanent) right gill slit.
		Left.	2d permanent left visceral cleft.		1st permanent left visceral cleft.		3d (2d permanent) primary gill slit.

deny its gill-cleft nature (Dohrn), van Wijhe regards it as a visceral cleft on the left side, antimeric to the club-shaped gland, which with Willey he regards as a modified visceral cleft, exactly homologous with the hyomandibular (spiracular) cleft of Craniota. Van Wijhe ('93, p. 155) finds evidence of a primary unpaired mouth in the external opening of the left anterior entodermic diverticulum known as the pre-oral pit (Räderorgan). Homologizing the "Gehirnanschwellung" of Amphioxus with the "Gehirnblase" of the larvæ of Ascidians, he considers it impossible to homologize the mouth (tremostoma) of Amphioxus with the median dorsal mouth of Tunicates, since in the former the mouth and its antimeres are laid down immediately *posterior* to the brain vesicle, whereas in the latter the mouth arises in the median plane immediately *anterior* to the brain vesicle; however, the *visceral clefts* of the young Ascidian larva are laid down, like the mouth of Amphioxus, immediately behind the brain vesicle. Moreover, van Wijhe holds that the mouth of Amphioxus is an organ of the left side only, and on the following grounds (quoted from Willey, '94, p. 178): "The outer muscle of the oral hood represents the anterior continuation of the *left half only* of the transverse and subatrial muscles. The inner nerve-plexus of the oral hood is formed on both sides exclusively from nerves which arise from the left side of the central nervous system. The velum is innervated entirely from nerves of the left side," viz. branches from the 4th, 5th, and 6th left dorsal nerves.

Willey ('94) finds evidence to support his view, that the mouth of Amphioxus represents the median dorsal mouth of Ascidians, in the marked asymmetrical conditions of the larva, for which van Wijhe's observations and conclusions afford no explanation. Affirming the asymmetry to be non-adaptive and non-advantageous (*contra* Korschelt und Heider), he concludes that it is the mechanical result of the (phylogenetic) forward extension of the notochord, an extension which is advantageous to an animal which bores in the sand. Hatschek ('92) and M. Fürbringer ('97) agree with Willey in this explanation as to the homology of the mouth of Amphioxus, but bring forward no evidence to support their view. There is no disagreement in homologizing the anterior entodermic diverticula (vordere Entodermsäckchen) of Amphioxus with at least part of the premandibular head cavities (1st somite of van Wijhe) in Craniota.

From the foregoing review it will be seen that two very important questions concerning the nature and homologies of the Vertebrate mouth remain in dispute, viz.:—1. Is or is not the mouth of Amphioxus to be

homologized with the mouth of Ascidians? 2. Is it or is it not homologous, either wholly or in part, with the mouth of Craniota? Upon the answer to the former question would seem to depend the settlement of the question whether the mouth of Amphioxus may or may not be regarded as a visceral cleft, for there is no reason to believe that the mouth of Ascidians represents a pair of visceral clefts. Notwithstanding that Willey appears to have in the asymmetrical mouth of Amphioxus strong evidence in favor of his homology, which has also met the approbation of Marshall ('93), I consider the different relation of the Tunicate and Vertebrate mouth to the brain vesicle a very serious objection to his theory. Furthermore, the presence of a preoral intestine in Vertebrates, which in *Squalus* extends (morphologically) anterior to the infundibulum, — even to the neuropore, as does the intestine of Tunicates, — leads me to agree with Beard, Kupffer ('88 and '91), and van Wijhe ('94), that in the present mouth of Vertebrates we have a *neostoma*, and also that a *palæostoma* homologous with that of Tunicates must be sought in an anterior opening of the preoral intestine. Kupffer finds evidence of this *palæostoma* in the ectodermic invagination of the hypophysis towards the "Preoraldarm," while van Wijhe finds it in Amphioxus, as stated in the Table, in the actual opening of the preoral intestinal diverticulum of the left side as the preoral pit (Räderorgan).

Waiving the question as to which, if either, of these theories is correct, I regard the mouth of Ascidians as opening at the morphologically anterior end of the alimentary canal; for there appears to me nothing in the literature upon Tunicates to show the presence of a preoral intestine in these forms. The mouth of Appendicularia, which has no "preoral lobe," (though homologized by Willey with the preoral intestinal diverticula of Amphioxus and the premandibular cavities of Craniota,) has a terminal position.¹ According to Willey the method of formation of the preoral lobe in those Ascidians possessing such is as follows (p. 218): "When the larva first hatches, the entoderm and ectoderm are in contact with one another at the anterior extremity of the body, just as they are in the earlier stages. Soon, however, the ectoderm, with the adhering papillæ, springs away from the endoderm at this point, leaving a space into which the two lateral mesodermic

¹ Willey ('94, p. 277) writes: "Whatever the truth may be as to the precise systematic position and phylogenetic value of Appendicularia, one thing, to my mind, remains absolutely certain, namely, that it has descended from a form which possessed a preoral lobe, and that it has secondarily lost that structure."

bands force their way. In this way a special anterior portion of the body cavity, præoral and præenteric, is produced, and is at first completely filled by a compact mass of rounded cells derived from the mesodermic bands. . . . The anterior, or præoral portion of the body cavity, of which we have just traced the origin, is, and subsequently becomes in a still more pronounced way, the *cavity of the snout*, or *præoral lobe*."

On the other hand, the præoral "head cavities" of *Amphioxus*, which Willey homologizes with the "preoral lobe" of *Ascidian* larvæ, are formed, as stated by Hatschek ('81), from an abstricted portion of the præoral archenteron. The differences in the formation of these two structures, therefore, seem too striking to permit their being considered completely homologous with each other.

Evidence has already been given in this paper which, in my opinion, makes it impossible to homologize the præoral "head cavities" (anterior entodermic diverticula) of *Amphioxus* with the "premandibular head cavities" of *Craniota*. The morphologically anterior portion of the archenteron, the "anterior head cavities" (Platt), are the only structures in higher Vertebrates which, in my opinion, can be homologized with the "head cavities" of *Amphioxus*. Homologizing, therefore, the "anterior head cavities" in these two forms, I submit on the opposite page for comparison with *Squalus* the table of the anterior eleven segments in *Amphioxus* as I interpret them.

If we compare Tables III. (p. 253) and V., we find the following fundamental resemblances in the segments of *Squalus* and *Amphioxus*.

Of the component elements of the *first segment*, that which I have regarded as the somatic element, consists of paired cavities cut off from the anterior portion of the archenteron. Since in both cases these cavities represent ventral as well as dorsal and lateral portions of the archenteron, it is impossible to contend that they contain only the mesodermic element of the segment. It seems not improbable that potentially they represent also the visceral-pouch element between this and the following segment. The opening of the left of these in *Amphioxus* to the exterior as the præoral pit may be regarded as evidence favoring this view. Moreover, M. Fürbringer ('97, p. 633) finds a late differentiated and rudimentary myotome, which lies anterior to the dorsal paired nerves II, which would, if present as stated by him, represent the mesodermic element of this segment, and the "anterior head cavities" would in consequence necessarily be regarded as modified or abortive visceral pouches, as held by Kupffer. Since my sections of *Amphioxus* give me no evidence of this rudimentary myotome, I hold

TABLE V.—METAMERISM OF AMPHIOXUS.

SEGMENTS	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	
Somites	{ a ¹ lost		{ 1	{ 2	{ 8	{ 4	{ 5	{ 6	{ 7	{ 8	{ 9	{ 10	{ 11
Dorsal nerves	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	
Ventral nerves		1	2	3	4	5	6	7	8	9	10	11	
Visceral clefts (r.)	lost	lost	c.s.g. ²	lost	1*	2*	3*	4*	5*	6*	7*	8*	
" " (l.)	lost	lost	M. ³	1	2*	3*	4*	5*	6*	7*	8*	9*	

¹ Possibly representing also a visceral-pouch element.² Club-shaped gland.³ M. Mouth.

The permanent visceral clefts are indicated by asterisks.

with van Wijhe, Hatschek, and Willey, that the first myotome in *Amphioxus* is situated behind the first two pairs of nerves, and also that the "anterior head cavities" of *Amphioxus* represent the somatic elements of the anterior segment in Craniota. From this point of view, the different fates which the two cavities in *Amphioxus* undergo, as well as the loss of musculature, is to be regarded as cœnogenetic. The dorsal nerves in both forms are exclusively sensor in correlation with the loss of splanchnic musculature.¹ The unpaired olfactory of *Amphioxus* is to be compared with the long persisting median connection of the neural tube and olfactory plate in *Squalus* (*lobus olfactorius impar*, Kupffer). No somatic musculature and no ventral nerves are developed. I regard the cerebral vesicle of *Amphioxus*, since it is limited posteriorly by the tuberculum posterius (Kupffer), as homologous with the primary fore-brain of *Squalus*, and therefore as the neuromeric element of the first segment.² Whether or not the visceral cleft of this segment is represented in the "anterior entodermic diverticula" (anterior head cavities), I am not able to assert with any degree of positiveness. Fürbringer's discovery appears to favor this view.

In the *second segment* a well developed myotome and ventral nerve develop. In both forms the dorsal nerve of this segment appears to be exclusively sensor. In Myxinoids, however, the dorsal nerve (ophthalmicus profundus) has motor fibres, and it appears to me not improbable that such will be found in its homologue in *Amphioxus*.³ If the visceral-cleft element in this segment is not represented in the "anterior head cavities," this may be assumed to have disappeared phylogenetically. All the components of the *third segment* are present, viz. somatic and splanchnic musculature, dorsal and ventral nerves, and visceral clefts.

¹ The homology of the olfactorius (I) with the first paired nerve of *Amphioxus* has already been asserted by Owen (1866). The first paired nerve of *Amphioxus* according to Owsjannikow (1866) and Rabl ('89) is homologous with trigeminus; with r. orbito nasalis or r. I. trigemini (Huxley, 1874); with opticus (Schneider, '79); with part of trigeminus (Rohon, 1881, and Krause, 1888); with ophth. prof. trig. (Hatschek, '92); and with nervus apicis (van Wijhe, '98).

² Kupffer ('93) homologizes the cerebral vesicle of *Amphioxus* with the Vorhirn (Vorderhirn and Mittelhirn) of Craniota.

³ The second paired nerve of *Amphioxus* has previously been homologized with part of trigeminus by J. Müller (1842), W. Müller (1875), and Krause (1888); with trigeminus by Goodsir (1841); with trigeminus and vagus by Quatrefages (1845) and Owen (1866); with facialis by Owsjannikow (1867); with opticus by Hasse (1876); with part of trigeminus and with facialis by Rohon (1881); with acustico-facialis by Rabl ('89); with trigeminus exclusive of ophth. profundus by Hatschek ('92); and with ophth. profundus by van Wijhe ('93).

I regard the mouth of *Amphioxus* as homologous with the left half of the mouth of *Craniota* and the club-shaped gland as its antimerere. That the mouth of *Amphioxus* as an organ of the left side is exactly homologous with the left half of the mouth of *Squalus* appears to me probable on the *a priori* ground that it is improbable that an organ of the same function should be twice acquired in the Vertebrate series; and also because the region of fusion of endoderm and ectoderm to form the mouth cleft is in both these forms ventral to the constrictions which separate the second and third mesodermic segments (1st and 2d myotomes). The club-shaped gland also appears as an entodermic diverticulum below the constriction between the second and third mesodermic segments of the right side, that is, opposite the mouth diverticulum, and I therefore, in agreement with van Wijhe ('93), regard it as the antimeric gill cleft.¹

In the *fourth segment* the following points of resemblance are to be noted. Somatic musculature and a somatic ventral nerve are present. While in *Squalus* the pair of visceral clefts which bounded anteriorly the splanchnic portion of this segment have disappeared, leaving no trace behind except in the neuromere with which they were connected, in *Amphioxus* only the right visceral cleft has been thus lost. The left visceral cleft, however, disappears ontogenetically without leaving a trace behind it. A further difference in the two forms appears in the fact that, whereas in *Squalus* the dorsal nerve has disappeared (or fused with the trigeminus), the dorsal nerve of the left side in *Amphioxus* is the first of the nerves which innervate the musculature of the velum (van Wijhe).

With the *fifth segment* in both forms begin the permanent visceral clefts. In agreement with Willey ('94), I regard the first secondary cleft as antimeric to the second primary cleft. Their fusion with the ectoderm below the mesodermic constriction between mesoderm segments 4 and 5 (myotomes 3 and 4) is the evidence for their relation to this, the fifth segment. I therefore consider *the first pair of permanent visceral clefts in Amphioxus as the exact homologues of the hyomandibular clefts of higher Vertebrates*. As has already been stated by Willey ('94), all except eight of the primary clefts (starred in the table), which become paired with eight antimeric clefts, undergo atrophy. In conse-

¹ Willey ('94) gives reasons for regarding the club-shaped gland as the antimerere of the first primary visceral cleft. His reasons are based on topographic relations in stages when the primitive topographic relations are considerably changed, and they seem to me less strong than the reasons stated by van Wijhe and myself.

quence there is found at the end of the larval period a "critical stage" of considerable duration, when *Amphioxus* possesses eight visceral clefts, which, if the homology above be correct, are exactly homologous with the eight morphological clefts of *Heptanchus* (Selachian) and *Petromyzon* (Cyclostome). The evidence of the exact homology of the mouth and visceral clefts of *Amphioxus* at its critical period with those of *Craniota* appears to me strongly confirmatory of the truth of the exact homology of segments in *Amphioxus* and *Squalus* as stated above.

i. GENERAL CONCLUSIONS.

The exact numerical correspondence of neuromeres (encephalomeres) and somites has been found not to be a purely accidental one. The ventral motor nerves (oculomotorius and trochlearis) of two successive encephalomeres, viz. II and III, are connected with two successive somites, viz. van Wijhe's 1st and 2d, and the nerves VII, IX, and X (Urvagus), by their topographic relations to successive somites 4, 5, and 6, show a similar metameric correspondence between encephalomeres and somites. Where correspondence does not clearly exist to-day, as in the case of the abducens nerve, we have developmental evidence which suggests how such modifications may have taken place.

Thirteen years ago Ahlborn ('84*), as a result of his examination of the evidence presented by van Wijhe ('82), stated it as his conclusion that in the head we have a dysmetamerism of neuromeres, which no longer repeats the metamerism of the mesomeres (somites), but is related to a series of other conditions dependent on both ectoderm and entoderm. Ahlborn likewise concluded that branchiomeres and mesomeres do not correspond. "Gegenbaur's assumption, that the segmentation of the cranial nerves, related as they are to visceral arches, is comparable to the segmentation of the spinal nerves, which correspond with somites, still remains to be proved." The evidence presented above certainly tends to make the assumed correspondence of mesomerism and branchiomeres more probable, and thus indirectly to prove the homodynamism of the nerves which innervate mesomeres and branchiomeres. The recent evidence presented by Hatschek ('92), Kupffer ('91, '96), Price ('96), and Miss Platt ('97) from their studies on *Amphioxus*, *Cyclostomes*, and *Amphibia* points in the same direction, and thus favors Gegenbaur's assumption. The comparative embryological evidence which has been given shows, however, that the adoption of Gegenbaur's view by no means necessitates the assumptions later made by him ('87),

viz.: (1) that the head primitively ended with van Wijhe's 6th somite;¹ (2) that between this and the following somite segments (dorsal as well as ventral) have been phylogenetically lost; and (3) that the head primitively ended with the gill region. It has been shown, I believe, that the probable phylogenetic and actual ontogenetic disappearance of visceral clefts does not necessitate the loss of the corresponding mesomere and neuromere. It is true that we have very good reason to infer a phylogenetic loss of distinctly differentiated somites and neuromeres in the Vertebrate series. It is also true that we find evidence of an ontogenetic disappearance of mesomeres. Nevertheless such evidence does not prove that somites have been phylogenetically lost from the occipital region before the group of Selachii, of which *Squalus* is one of the most primitive forms, is reached. I believe that the evidence which has been given of the complete metameric correspondence of neuromeres and mesomeres—that the Selachian embryo is in this respect an unbroken continuum—renders it unnecessary to assume that somites have been so completely lost that no traces of them appear phylogenetically in Selachii. It is no longer necessary to assume a palingenetic portion of the Vertebrate head which ended with the sixth visceral arch of Selachii (Gegenbaur), or an exact homology between the hypoglossus roots (surely a most uncertain "fixed point") of adult Vertebrates (M. Fürbringer). The evidence which I have given seems thus to favor the opinion of Sewertzoff ('95), that we have "keinen Grund, vorauszusetzen, dass zwischen den palingenetischen Somiten v. Wijhe's (I–VI) und den coenogenetischen (VII–IX) ein Wegfallen der Segmente stattgefunden hat. Wir sehen eine vollkommen regelmässige Anlage der Kopfsomiten und ein eben so regelmässiges [ontogenetic] Verschwinden derselben."

I am aware, however, that the structural differences between the hind-brain neuromeres, e. g. IV to VII, and the neuromeres immediately

¹ The suggestion that the gill region is not confined to the head region was first made by Huxley ('58). I believe that direct evidence in favor of this suggestion is furnished by *Amphioxus* (Hatschek, '92), and by *Myxinoidea* (Price, '98). In this connection, moreover, it is of interest that in my previously ('97) made homology the last visceral cleft in *Ammocoetes* primitively bounds *posteriorly* the segment which is homologous with the last cranial segment (Hoffmann, '94) of *Squalus*, viz. van Wijhe's 10th somite. Furthermore it has been shown (p. 268) that this last visceral cleft of *Petromyzon* is exactly homologous with the last visceral cleft of *Amphioxus* in its "critical stage" of development. It should, however, be noted that there have been published three other interpretations of homologies between Selachii and Cyclostomata, differing from that made by me, viz. those by Ahlborn ('84*), by Hatschek ('92), and by Sewertzoff ('95).

following these may seem to favor Gegenbaur's view that the former belong to a palingenetic portion of the Vertebrate head which ended with the 6th (van Wijhe's) somite (bounding neuromere VII posteriorly and ventrally). The structural gap between the seventh and eighth neuromeres is not, however, so sharp that it should outweigh evidences of similarity, and especially the evidence that somites 6 and 7 are indisputably serially homologous. I must confess that I cannot see that the assumption of palingenetic and cœnogenetic portions of the Vertebrate head has added to the clearness of our morphological conceptions, nor can I see that it is rendered necessary by any ontogenetic or phylogenetic evidence now in our possession. Note, furthermore, the disagreement of opinion as regards what is and what is not *palingenetic* or *cœnogenetic* among those who have been prominent as advocates of this view, viz. Gegenbaur ('87), his pupil, Fürbringer ('97), and Miss Platt ('97). While Gegenbaur holds that van Wijhe's 6th somite is palingenetic, Fürbringer regards the 6th, and possibly the 5th and 4th somites, as *cœnogenetic*. Miss Platt, on the other hand, believes that the 4th and 5th somites are palingenetic, but that the 6th somite is probably cœnogenetic. All this appears to me confusing and unnecessary. The terms cœnogenetic and palingenetic are purely relative terms. I hold the view that each metamere of the head may be regarded as cœnogenetic in comparison with the metameres anterior to it, the head gradually receiving accessions from the trunk. Gegenbaur's famous "Kritik" of 1887 appears more an attempt to establish the visceral arches as the *essential* criteria of cephalic metameres, than a wholly unprejudiced effort to weigh the evidence both anatomical and embryological which was at his command. I believe that the evidence given in the present paper tends to strengthen the generally accepted opinion, which Gegenbaur has sought to overthrow, that the mesomeres in the head, like those in the trunk, afford the most trustworthy criteria of metamerism. The dorsal (neuromeric and mesomeric) segmentation must be regarded as more conservative than the ventral (branchiomeric or splanchnic) segmentation. The lost elements are chiefly the ventral ones. Their loss has indirectly caused the losses in the dorsal elements, such as the disappearance of splanchnic motor fibres from dorsal nerves and (?) of the thickening of the lateral zones of encephalomeres I and II.

It appears to me that the evidence now in our possession gives reason to hope for an eventual solution of the head problem, not only as regards the nature, but also the number of head segments. The problem, it is

true, is easier for occipital than for pre-occipital segments. The serial homology of occipital with trunk segments is not generally questioned at present. A comparison of the integral parts of occipital and trunk metameres shows that the belief in their serial homology is well founded. It must, however, be admitted that occipital metameres show no evidence of either excretory or reproductive organs. Nevertheless we may readily believe from the evidence of these organs in the gill region of *Amphioxus* that this is a cœnogenetic loss in the Vertebrate series. The chief grounds for belief in the homology of trunk and occipital metameres are these: (1) Occipital somites with their (2) ventral nerves are undoubtedly the serial homologues of trunk somites with their ventral nerves. This evidence alone has convinced most morphologists. But there are still other reasons. With our present knowledge, we may, I think, affirm that (3) dorsal occipital (or cranial) and dorsal spinal nerves are serial homologues. One by one, since the discovery by Schneider ('79) of ventral nerves in *Amphioxus*, the differences between dorsal spinal and cranial nerves, which were at one time or another maintained, have been with increased comparative embryological and anatomical knowledge shown to be unessential. The evidence given by Schneider ('79), Hatschek ('92), and van Wijhe ('93) shows that dorsal nerves, as seen in *Amphioxus*, are mixed in function, innervating the skin and splanchnic musculature, while ventral nerves are motor in function, innervating somatic musculature. The typical cranial nerves of Craniota, viz. V, VII, IX, and X, are morphologically comparable with the dorsal nerves of *Amphioxus*, and are therefore to be regarded, as Balfour for other reasons regarded them, more primitive than the *spinal* nerves, which lack the lateral and dorsal (except in Cyclostomes) cutaneous branches.¹ The recent researches of von Lenhossék ('90), Ramon y Cajal, and Kölliker, by demonstrating the existence of non-ganglionic fibres in the dorsal spinal nerves of Craniota, which by their relations must be regarded as motor in function, have shown that in this respect spinal nerves do not differ from cranial. Moreover, in view of the evidence given by Goronowitsch ('92), Sewertzoff ('95), Neal ('97), and Miss Platt ('97), it can no longer be

¹ The place of these branches has been usurped by the lateral branches of the vagus, as I believe has been suggested by Eisig. The advantage in greater centralization is obvious. If it be true, and it is generally admitted, that cranial nerves receive cells from the skin while the spinal nerves do not, an explanation of this also is seen in the extension of the vagus and the concomitant loss to spinal nerves.

truthfully said that cranial nerves differ from spinal in that the former extend laterad and the latter mediad of the mesomeres. We must conclude that dorsal nerves were in all probability, as in *Amphioxus*, related to the septa between myotomes. Finally, the distinction made by His, in the case of dorsal cranial nerves, between dorsal (sensor) and lateral (motor) *roots*, has, with the knowledge of the facts above stated, an anatomical and physiological rather than a morphological interest. I therefore see no escape from the conclusion that the occipital region of the head is not a region *sui generis*, and I pass to the consideration of the pre-occipital segments.

To those who are deeply impressed with the differences between post-otic and pre-otic regions of the Vertebrate head, it is necessary to emphasize the following fundamental resemblances in the segments of these two regions. (1) Pre-otic and post-otic encephalomeres have been shown to be morphologically comparable. (2) The dorsal nerves connected with these, and (3) the visceral arches which these nerves supply are in these two regions serially homologous. Moreover, as evidence pointing in the same direction, it may be stated that (4) a post-otic nerve innervates pre-otic musculature. Furthermore, the serial homology of pre-otic and post-otic somites appears established by the fact that (5) a pre-otic somite (van Wijhe's 3d somite) is a segment of the dorsal mesoderm. That it is such seems clear, for it is defined anteriorly and posteriorly by well marked constrictions (observed by several investigators), it becomes differentiated into myotome and sclerotome, and its musculature appears first in its median wall, and becomes innervated by a ventral nerve (*abducens*) serially homologous with ventral spinal nerves. The fact that the primitively dorsal mesoderm of the pre-otic region grows ventrally to form the splanchnic musculature, as has been stated for Cyclostomes, Selachii, and Amphibia, is not a basis for a fundamental distinction between post-otic and pre-otic regions, since this is the method of formation of splanchnic mesoderm throughout the length of the body in *Amphioxus*. In this respect, as in respect to the nerves, the head shows more primitive conditions than the trunk. Since the literature of the last decade and a half shows little agreement of opinion as to the morphology of the eye-muscle nerves, more especially the oculomotorius and the trochlearis, and since in the preceding pages evidence has been given which tends to reconcile existing differences, it is important to consider briefly the bearing of their morphology upon that of the pre-otic segments. The more recent attempts to classify the eye-muscle nerves as dorsal,

lateral, or ventral indicates that the point of view of morphologists is now fundamentally different from that of the older anatomists, who, in dealing with the question of the segmental value of cranial nerves, excluded the eye-muscle nerves from consideration on the ground of their inconstancy in appearance and distribution. Except on the part of Froriep, Kastschenko, and Rabl, who regard the pre-otic region as one *sui generis*, I find no tendency to revert to the view of Stannius ('49, p. 125) that "der Parallelisirung der Augenmuskelnerven mit Spinalnerven stellen sich, wegen ihrer eigenthümlichen Ursprungs-verhältnisse, des ihnen zukommenden Mangels von Ganglien und der ausschliesslichen Vertheilung ihrer ungemischten Primitivröhren in den, auch ihrerseits mit Muskeln der Wirbelsäule durchaus nicht vergleichbaren, Muskeln eines Sinnes-Apparates so unüberwindliche Schwierigkeiten entgegen, dass von einer solchen nicht füglich die Rede sein kann." However, the labors of comparative anatomists, among whom may be named Huxley, Gegenbaur, M. Fürbringer, and Schwalbe, during the thirty years following the work of Stannius just quoted, resulted in so well establishing the "Bürgerrecht" of the eye-muscle nerves that morphologists now assume that they are comparable with either dorsal or else ventral segmental nerves. Only a minority of anatomists, among whom may be named Schneider ('79), van Wijhe ('82), Beard ('85), His ('88*), Dohrn ('91), Neal ('96), and M. Fürbringer ('97), have regarded them as ventral segmental nerves. The weightiest well established evidence in favor of this view was first stated by His ('88), and consists in the fact that the eye-muscle nerves, at least of the adult, resemble ventral spinal nerves both in histological structure and in the situation of their motor nucleus in the ventral horn of the neural tube; and also in the less well established fact that they innervate musculature derived from segments of the dorsal mesoderm. On the other hand, the majority of morphologists, among whom may be named Bal-four ('78), Marshall ('81), Dohrn ('85, '87, '90), Gaskell ('89), Hoffmann ('89, '94), Oppel ('90), Houssay ('90), Platt ('91), Froriep ('91), Zimmermann ('91), Hatschek ('92), Mitrophanow ('92, '93), and Kupffer ('94, '95, '96), while in general of the opinion that the abducens is the homologue of one or more segmental ventral nerves, have held that either the trochlearis or the oculomotorius, or both, represent dorsal (or lateral) segmental nerves. The chief arguments in favor of this view consist in evidence (1) of the development of these nerves from neural-crest cells; (2) of a cellular or so called ganglionic structure of the nerves in the embryo; (3) of transitory or permanent ganglia in con-

nection with them; and (4) of the development of at least a part of the musculature innervated by them from splanchnic mesoderm. Thus there is to-day a distinct conflict as to the morphology of the eye-muscle nerves, one party to the conflict being supported by histological evidence, the other by embryological. The assumption by His ('88), that the eye-muscle nerves develop as processes of medullary cells (neuroblasts), — which is involved in his contention that they are the serial homologues of ventral spinal nerves, — has never hitherto received the requisite embryological confirmation. In fact, the latest embryological evidence concerning the development of the oculomotorius and trochlearis seems quite irreconcilable with the view of Schneider ('79), van Wijhe, and His. In regard to the latter nerve, Hoffmann ('89, p. 338) says, if one disregards the fact that no ectodermal fusion takes place, "so gleicht die Anlage des Trochlearis in sehr jungen Entwicklungsstadien [of *Lacerta*] vollkommen der eines segmentalen Kopfnerven, besonders der des Trigeminus." Froriep also finds that the trochlearis possesses in early stages a ganglion, and is differentiated from neural-crest cells *in situ*. Miss Platt ('91*, p. 259) likewise states that "in *Acanthias* the development of the trochlearis in all essential respects so completely corresponds to that of the trigeminus and facialis, that like them it must be considered to combine primarily those dorsal and ventral elements which have separate roots in the nerves of the trunk. It can, therefore, not be regarded as the ventral root of another segmental nerve." Moreover, Kupffer ('95, '96) finds the trochlearis to possess in *Ammocetes* both dorsal and ventral roots.

With regard to the oculomotorius, the conclusions of embryologists are even more conflicting. While Dohrn ('91) finds that this nerve is formed by the migration of cells from the ventral wall of the midbrain, and considers it a motor nerve, Miss Platt ('91*) states that she has shown the oculomotorius to be "undoubtedly originally sensory." Her observation that the nerve develops from the ganglion toward the brain has been confirmed by both Mitrophanow ('93) and Sedgwick ('95). Nevertheless the evidence which has been stated by me in division VI. shows conclusively, as I believe, that all the eye-muscle nerves, oculomotorius, trochlearis, and abducens, develop, like ventral spinal nerves, as processes from neuroblasts lying in the ventral horn of the medullary tube. Therefore, from their development, as well as their adult histological structure and relationships, the eye-muscle nerves must be regarded as the serial homologues of ventral spinal nerves. Finally, with the accumulating evidence given by many investigators, — among

them Beard, Dohrn, Ayers, and Kupffer, — that the complicated sensory organs of ear, eye, and nose are differentiations of lateral-line sense organs, we may conclude that there exist no fundamental differences in *nature* between pre-otic and post-otic segments.

The *number* of cephalic segments in the post-otic region (Sewertzoff, Fürbringer) appears to be variable in different Vertebrates. If the estimate given by Hoffmann ('94) for *Squalus* be correct, there are six post-otic cephalic segments in that form. In the otic and pre-otic regions, I hold the number to be not greater than six,¹ and the exact numerical correspondence of neuromeres and somites very strongly supports the estimate of six, which accords very closely with that made, upon similar but not identical grounds, by van Wijhe, Beard, Marshall, and Miss Platt. I cannot agree with Hoffmann ('96) and M. Fürbringer ('97), who — from the evidence that there is one more mesodermal segment (*viz.* the "anterior") in *Squalus* and *Galeus* than in other known Selachian embryos — conclude that still other anterior mesodermal segments have phylogenetically disappeared, and that it is therefore impossible for us to estimate the number of pre-otic segments. *We have quite as little reason to believe that somites anterior to Platt's have disappeared, as we have to believe that encephalomerus anterior to encephalomere I (the primary forebrain) have once existed.* In the exact numerical correspondence of neuromeres and somites we have, not only evidence of the serial homology of head and trunk segments, but the means to determine their number in the pre-otic region.

IX. Summary.

I am unable to regard Locy's "neural segments" as segments in the true sense of the word, because I find them irregular in size, inconstant in number, bilaterally asymmetrical, and without definite relation to structures known to be segmental. They are phenomena connected with the proliferation and disassociation of the cells of the neural crest.

The posterior boundary of the cephalic plate coincides with the posterior boundary of encephalomere VI, opposite which the auditory invagination takes place.

Orr's criteria for hindbrain neuromeres hold good only for the later

¹ Six neuromeres alternating with five somites. With Miss Platt ('94) I hold that the otic sense organ was primitively situated above the constriction between van Wijhe's 4th and 5th somites.

stages of development of *S. acanthias*. In the early stages of this animal, the neuromeres are local thickenings of the lateral zones, as well as dilatations of all of the zones of the medulla. As paired glangionic enlargements of the central nervous system, they obviously resemble, except in position, the ventral chain of ganglia of Annelida. Therefore they cannot be explained as the passive result of mechanical shoving or bending. The constrictions between the neuromeres, as well as the crowding of nuclei in the regions of constriction, may however be, and most probably are, intensified by shoving or bending of the neural tube.

No structural conditions are presented by the myelomeres which are not reconcilable with the hypothesis that their existence is dependent upon the presence of the mesodermal somites. If they ever possessed a dorsal segmentation like that of the "hindbrain neuromeres," — and there is no evidence to show that they ever did, — it has been lost. But, though they appear of doubtful morphological value, their numerical correspondence with nerves and somites attests their metameric value.

The so called neuromeres of the forebrain and midbrain (encephalomeres of Zimmermann) are not morphologically comparable with "hindbrain neuromeres," since they are simply dorsal or ventral expansions which are secondary in the time of their appearance. I hold that there are much better reasons — viz. on the grounds of time of appearance, of structure, and of relation to nerves and somites — for regarding each of the primary forebrain and midbrain vesicles (neuromeres I and II) as serially homologous with hindbrain neuromeres (neuromeres III to VII), than for so regarding their later subdivisions. The latter are cœnogenetic vesiculations of the neural tube, and not of metameric value.

Both dorsal ganglia and ventral nerves in the trunk develop in the regions of constriction between myelomeres. A comparison with the conditions in *Amphioxus* and *Petromyzon* shows that this condition is not to be regarded as primitive, but that previously dorsal and ventral nerves alternated, the former being intersomitic in position. Such topographical relation is retained by some cranial nerves, viz. V, VII, IX, and X (*Urvagus*).

The ganglionic Anlagen of four cranial nerves, viz. V, VII, IX, and X, are proliferated from four encephalomeres, viz. III, V, VI, and VII. Chiefly for this reason, but also because of the clear connection of two splanchnic motor roots, viz. V and VII, with two of the encephalomeres, I conclude that the primitive metameric relations of the latter were with the visceral arches. The local thickenings of the hindbrain neuromeres

(encephalomeres) may be considered as the primitive nervous centres of nerves which corresponded numerically with visceral arches. If they were such, then one of the encephalomeres (IV) affords evidence of a lost visceral arch.

Although the structure of myelomeres and encephalomeres is seen to be different, yet in the stages of embryonic development, where both are present, the latter are seen to have segmental value from the fact that corresponding with them there is an equal number of somites. These somites, as exemplified in the 3d (van Wijhe's), are morphologically comparable and serially homologous with trunk somites. I conclude, then, that there was a primitive correspondence between neuromerism, mesomerism, and branchiomerism.

The development, histological structure, and relationships of the eye-muscle nerves (III, IV, and VI) show them to be the serial homologues of ventral spinal nerves. Like the latter (His), they develop as axis-cylinder processes of neuroblasts in the ventral horn of the neural tube.

Pre-otic and post-otic metameres, like their integral parts, are serially homologous with one another. Therefore, if the latter are serially homologous with trunk metameres the former must be also. Table III. (p. 253) summarizes my opinion as to the primitive composition of metameres I to VII. I regard the r. ophthalmicus profundus as a segmental dorsal nerve belonging to metamere II, while the oculomotorius is its ventral root. The trochlearis is the ventral nerve of metamere III, and the abducens represents the ventral nerves of metameres IV to VII.

There are five mesomeres alternating with six neuromeres in the otic and pre-otic regions of the Vertebrate head. Probably eleven neuromeres are finally included in the head of *Squalus*. The evidence of the numerical correspondence of neuromeres and mesomeres shows that there is no more reason for believing that somites have been lost anterior to Platt's (anterior) somite, than that neuromeres have been lost anterior to the primary forebrain.

In agreement with van Wijhe, I homologize the mouth of *Amphioxus* with the left half of the mouth of *Craniota*. The first pair of permanent visceral clefts in *Amphioxus* are exactly homologous with the hyomandibular clefts of higher Vertebrates. The eight visceral clefts possessed by *Amphioxus* at its "critical stage" (Willey) are exactly homologous with the eight morphological clefts found in some *Selachii* and *Cyclostomes*.

This investigation has been made in the Zoölogical Laboratory of the Museum of Comparative Zoölogy at Harvard College. I gratefully acknowledge the valuable assistance and advice of its Director, Prof. E. L. Mark, at whose suggestion the work was undertaken. I am indebted to Alexander Agassiz for the privilege of studying at his private laboratory in Newport; also to Professor Mark for embryonic material of *Petromyzon*, and to Miss Julia B. Platt for embryonic material of *Amphioxus*.

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DESCRIPTION OF PLATES.

All the drawings were made with the Abbé camera lucida. Figure 40 (Plate 6) is, however, a reconstruction from sections and dissected specimens. The Figures of Plates 8 and 9, with the exception of Figures 61 and 66, are also reconstructions from several sections. In sagittal sections, the embryo is always viewed from the right side. In cross sections, it is the posterior face of the section that is shown, so that right in the figure corresponds to right in the section. In frontal sections, the dorsal face is shown, so that right in the figure here also corresponds with right in the section. Only Figures 2 and 3 (Plate 1) represent embryos viewed from the ventral side, so that what appears on the left side in these two figures is really on the right side of the embryo. The cells of the neural crest are in all cases colored blue.

ABBREVIATIONS COMMON TO ALL FIGURES OF TEXT
AND PLATES.

*	Posterior limit of cephalic plate.	<i>coms. p.</i>	Posterior commissure.
<i>I-VII.</i>	Encephalomeres.	<i>coms. su.</i>	Superior "
<i>1-7.</i>	Somites (van Wijhe's).	<i>ec'drm.</i>	Ectoderm.
<i>2', 3'.</i>	Cavities of head somites 2, 3.	<i>en'drm.</i>	Entoderm.
<i>V. md.</i>	Ramus mandibularis trigemini.	<i>ent.</i>	Entoderm.
<i>V. mx.</i>	R. maxillaris trigemini.	<i>fis. vsc. 1-6.</i>	Visceral clefts 1 to 6.
<i>V. opt. su.</i>	R. ophth. superficialis trigemini.	<i>gls-phy.</i>	Glossopharyngeus nerve.
		<i>gn. ac-fac.</i>	Ganglionic Anlage of acustico-facialis.
		<i>gn. fac.</i>	Ganglion of acustico-facialis.
<i>V. opt. p'fnd.</i>	R. ophth. profundus trig.	<i>gn. Gas.</i>	Gasserian ganglion.
<i>V. rz. maj.</i>	Radix major trigemini.	<i>gn. gls-phy.</i>	Ganglion of glossopharyngeus.
<i>V. rz. min.</i>	" minor trigemini.	<i>gn. ms-ce.</i>	Mesocephalic ganglion.
<i>VII. ac.</i>	Ramus acusticus facialis.	<i>gn. trig.</i>	Ganglionic Anlage of the trigeminus nerve.
<i>VII. buc.</i>	" buccalis "	<i>gn. spi.</i>	Spinal ganglion.
<i>VII. hoi.</i>	" hyoideus "	<i>gn. vag.</i>	Ganglionic Anlage of the Vagus.
<i>VII. opt. su.</i>	" ophth. superficialis fac.	<i>i'fb.</i>	Infundibulum.
<i>a, β, γ.</i>	Position of frontal sections (Figs. 38, 87, 88).	<i>la. ct.</i>	Lamina cutis (cutis plate).
<i>aβ.</i>	(Fig. C.) Position of section (Fig. D).	<i>la. mu.</i>	Lamina muscularis (muscle plate).
<i>a.</i>	"Anterior cavity" (Figs. B, C, E). Ventral fibre tract (Fig. F).	<i>m-b.</i>	Midbrain.
<i>abd.</i>	Abducens nerve.	<i>mu. ob. su.</i>	Superior oblique muscle.
<i>ao. d.</i>	Dorsal aorta.	<i>mu. rt. su.</i>	" rectus muscle.
<i>arc. vsc. 1.</i>	Visceral arch 1.	<i>mu. rt. a.</i>	Anterior rectus muscle.
<i>ar'ent.</i>	Archenteron.	<i>my'cel.</i>	Myocœle.
<i>au.</i>	Auditory invagination (otic vesicle).	<i>myl-mer.</i>	Myelomere.
		<i>my-tm.</i>	Myotome.
<i>ax-cyl.</i>	Axis-cylinder process.	<i>n-po.</i>	Neuropore.
<i>brs. vsc. 1-6.</i>	Visceral pouches 1 to 6.	<i>oc-mot.</i>	Oculomotorius nerve.
<i>cav. a.</i>	Platt's somite (anterior cavity).	<i>pr'enc.</i>	Prosencephalon.
<i>cb.</i>	Anlage of cerebellum.	<i>rx. v.</i>	Ventral root of nerve.
<i>cd.</i>	Chorda dorsalis.	<i>so.</i>	Somite.
<i>cl. crs. n.</i>	Neural-crest cells.	<i>tb. n.</i>	Neural tube.
<i>cl. ms-ce.</i>	Cells of mesocephalic ganglion.	<i>thl.</i>	Thalamic portion of the trigeminus Anlage.
<i>cl. n'bl.</i>	Neuroblastic cell.	<i>trch.</i>	Trochlearis nerve.
<i>coms. a.</i>	Anterior commissure.	<i>vag.</i>	Vagus nerve.
<i>coms. d.</i>	Dorsal "	<i>vn. crd.</i>	Vena cardinalis.
		<i>vs. opt.</i>	Optic vesicle.

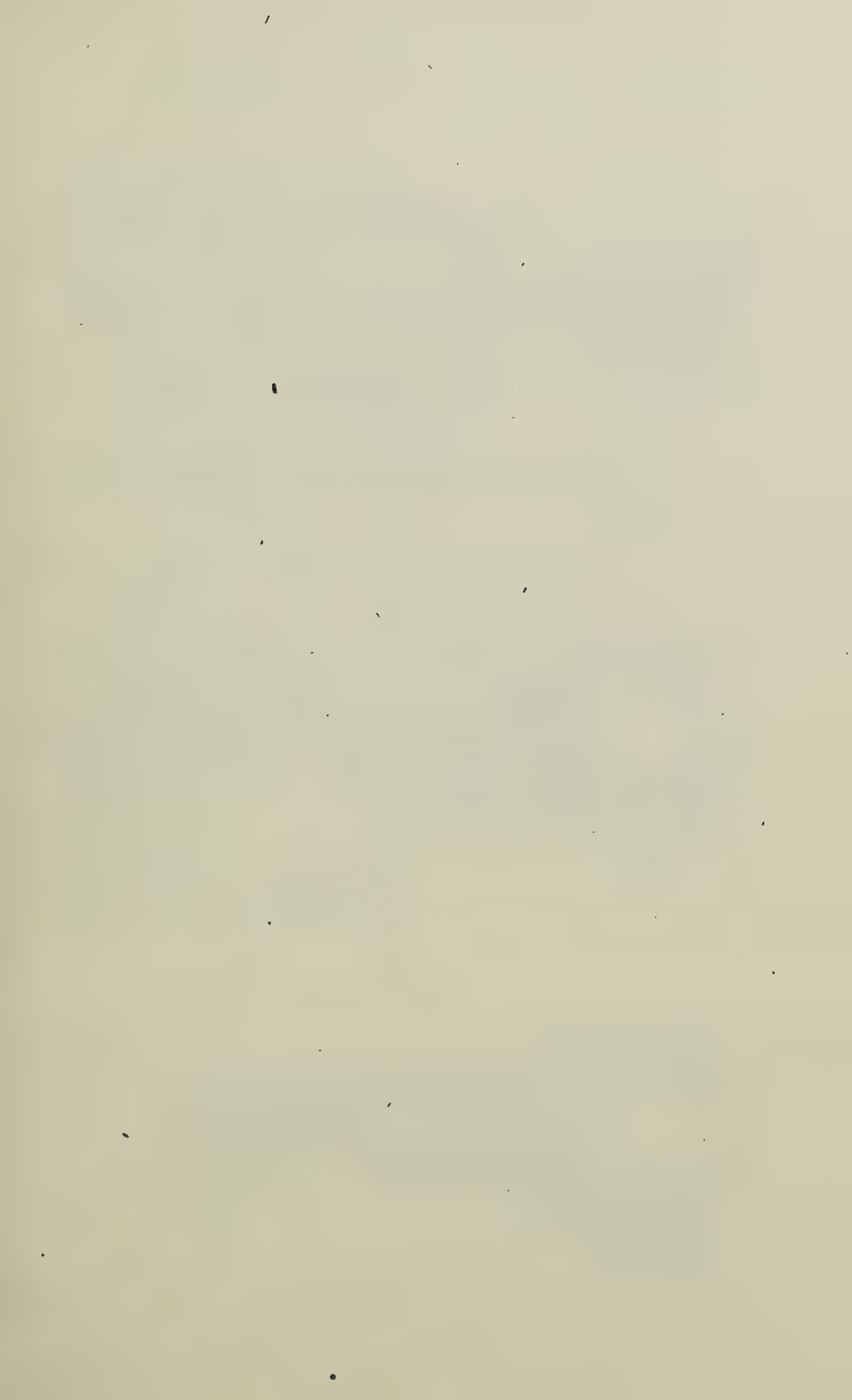
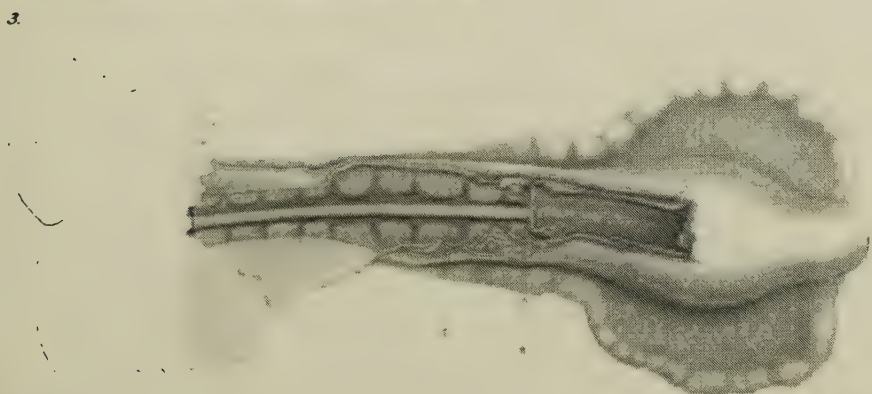
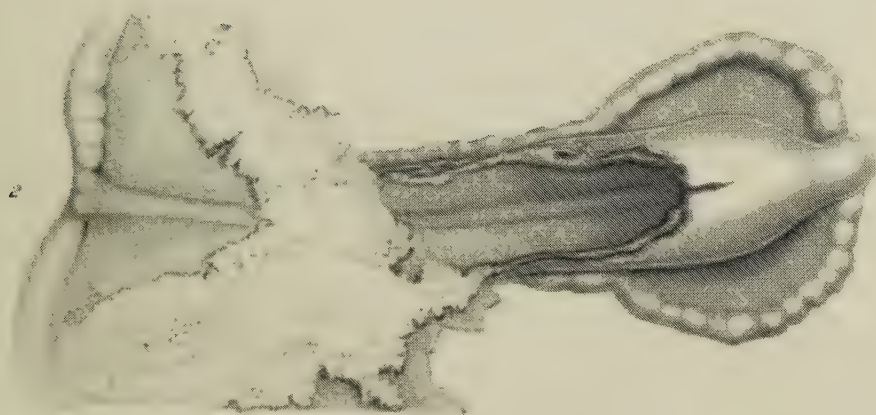
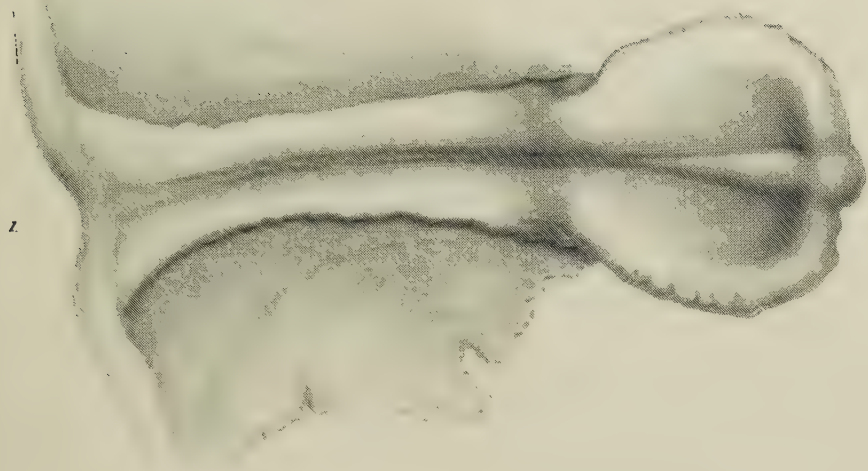


PLATE 1.

All figures magnified 43 diameters, and oriented on the plate with the chief axis horizontal, the anterior end of the embryo to the right. The embryo made translucent was drawn in outline with camera lucida and afterwards studied as an opaque object.

- Fig. 1. A dorsal view of an embryo with 6 to $6\frac{1}{2}$ somites. The edges of the neural plate are seen to be irregularly lobed. The two deep depressions at the anterior end of the cephalic plate mark the position of the future fundus of the infundibulum.
- Fig. 2. A ventral view of the same embryo. Locy's segments are seen as lobings of the ventrally recurved margin of the neural plate.
- Fig. 3. A ventral view of another embryo of the same stage of development. The specimen was dissected to show the chorda, a rod in the median axial line, on either side of which lie the somites, van Wijhe's seventh somite being designated as 7. An asterisk (*) marks the posterior boundary of the cephalic plate.



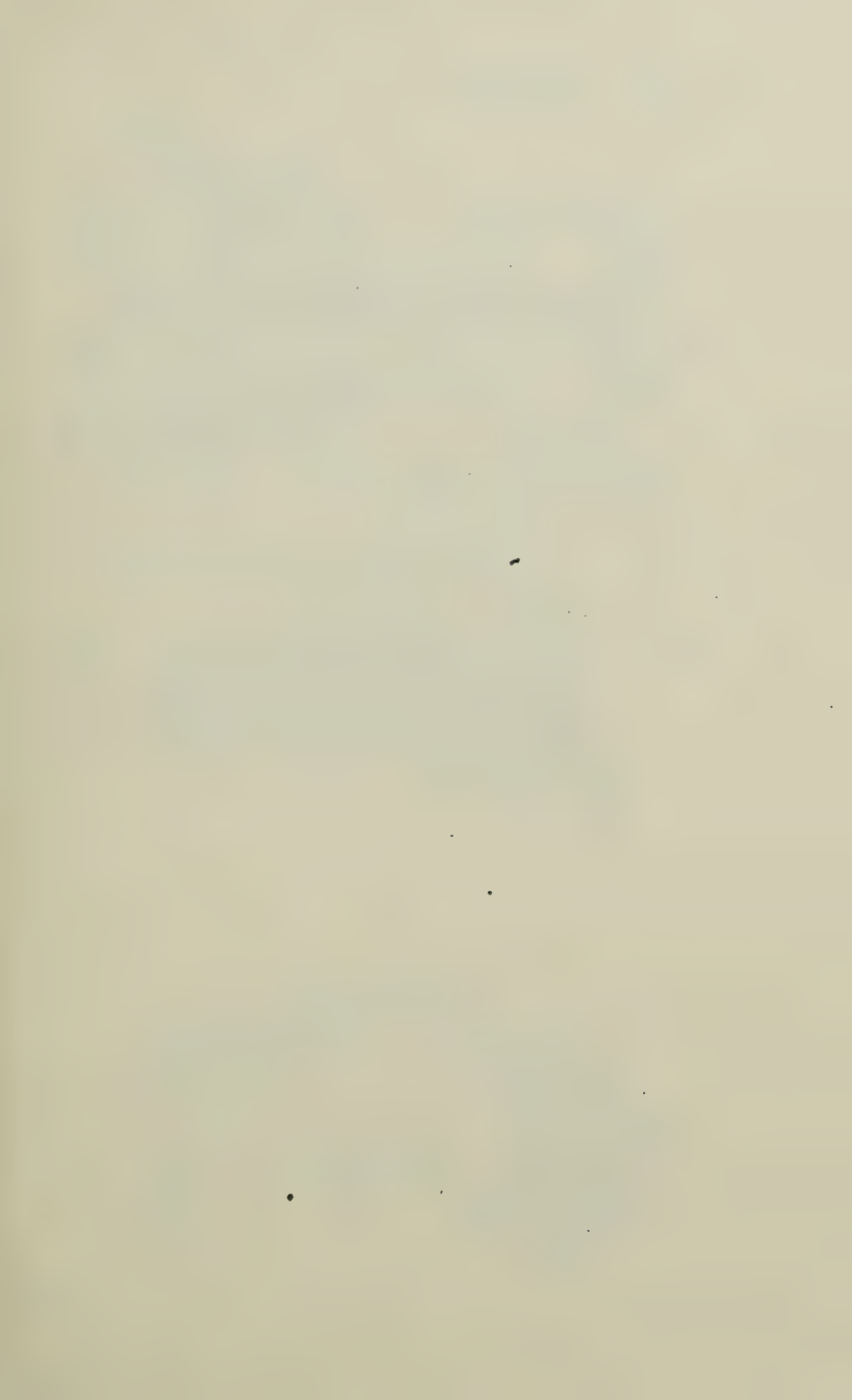
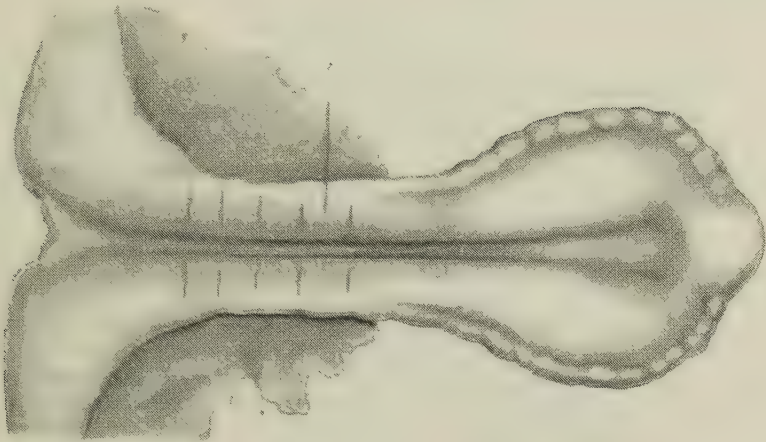


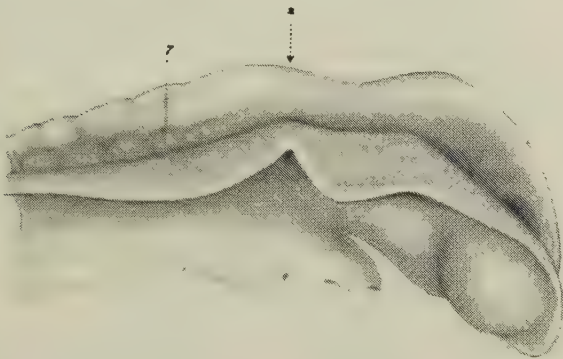
PLATE 2

All figures magnified 48 diameters and oriented as in Plate 1. The outlines were first made from the translucent embryos with camera lucida, and afterwards the embryos were studied as opaque objects.

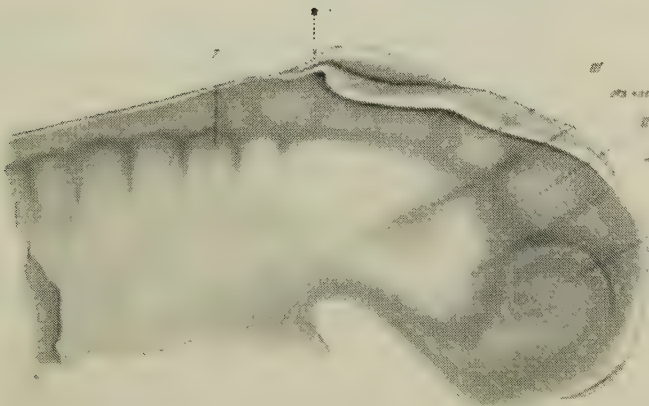
- Fig. 4. An embryo with 4 somites viewed from the dorsal side. Locy's segments are seen to be confined to the "marginal bands" of the cephalic plate.
- Fig. 5. An embryo with 10 or 11 somites viewed from the right side and partly from above. The posterior part of the cephalic plate is seen to be sharply flexed ventrad on the right side.
- Fig. 6. An embryo with 12 somites viewed from the right side. The neural folds in the region of the cephalic plate have not yet met in the mid-dorsal line. The demarcation between cephalic plate and trunk is seen to be sharp. The anterior three primary vesicles (encephalomeres I, II, and III) appear in surface study as shown in the figure. In neither this embryo nor in the one represented in Figure 5 do Locy's segments appear.



4



5

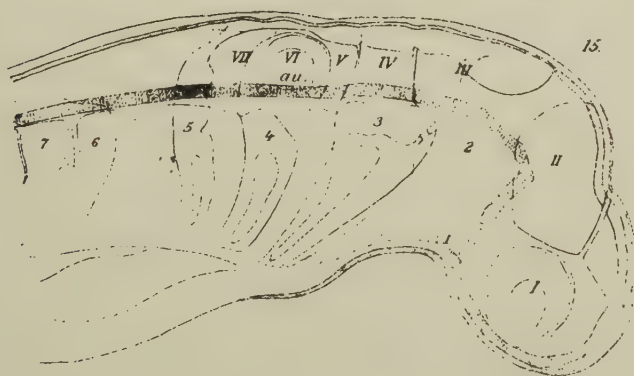
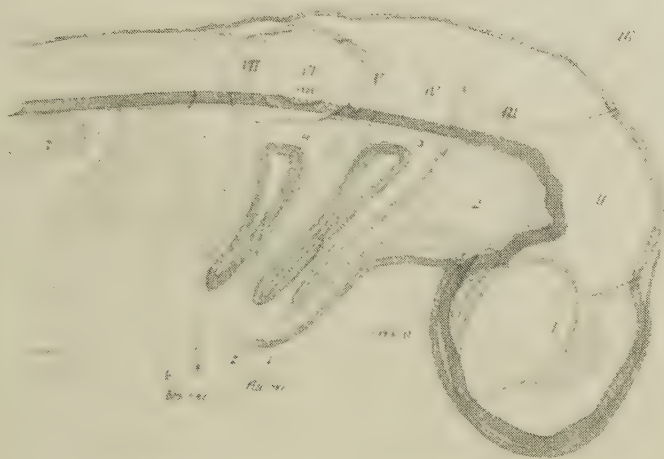
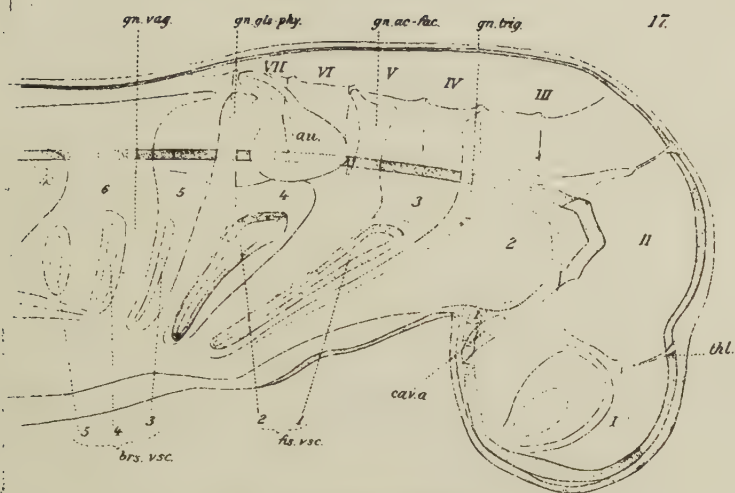


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PLATE 3.

All figures drawn from cleared specimens and magnified 43 diameters. The neural tube seen in optical sagittal section. Neural-crest cells (ganglionic Anlagen) colored in blue. In all cases the embryo is viewed from the right side.

- Fig. 7. An embryo with 14 to 16 somites. Six vesicles only appear, and these are included within the limits of the cephalic plate. Neural crest (trigeminus Anlage) differentiated in the region of encephalomeres II and III. The mesodermic constrictions dividing somites 1, 2, 3, and 4 have appeared. Two visceral pouches (1 and 2) are in the process of breaking through the lateral plates (splanchnic mesoderm).
- Fig. 8. Embryo with 18 or 19 somites. A thickening of the lateral zones in the posterior part of encephalomere III (not shown in figure) appears in sections of this stage. The acustico-facialis Anlage has become differentiated in the region of encephalomere V. The "anterior cavity" (Platt's) begins to be cut off from the mesoderm of the 1st somite (van Wijhe's).
- Fig. 9. Embryo with 19 or 20 somites. A dorsal expansion now appears behind VI, as the first indication of encephalomere VII. Posteriorly it is bounded by somite 6. The constriction between van Wijhe's 3d and 4th somites has become obscured by the migration of cells from both sides of the constriction to meet the advancing Anlage of the acustico-facialis.
- Fig. 10. Embryo with 21 or 22 somites. The conditions remain practically unchanged.
- Fig. 11. Embryo with 24 or 25 somites. A ventral migration of neural-crest cells in the region of encephalomere VI has now begun, and the crest is now differentiated in the region of encephalomere VII and posteriorly.
- Fig. 12. Embryo with 26 or 27 somites. A continuous neural crest extends from encephalomere V into the trunk region. Thalamic portion of the trigeminus Anlage clearly differentiated.
- Fig. 13. Embryo with 28 to 30 somites. At this stage all of van Wijhe's somites appear clearly differentiated. The Anlagen of the acustico-facialis and the glossopharyngeus, differentiated from encephalomeres V and VI, appear topographically related to the constrictions between van Wijhe's somites, 3-4 and 4-5.
- Fig. 14. Embryo with 33 or 34 somites. Trochlear portion of trigeminus Anlage (compare Fig. 21, *trch.*) clearly differentiated. The commissure connecting acustico-facialis and glossopharyngeus appears dorsal to the auditory invagination.
- Fig. 15. Embryo with 38 or 39 somites.
- Fig. 16. Embryo with 42 somites. Platt's "anterior somite" (*cav. a.*) clearly differentiated. The anterior cells of the vagus Anlage, proliferated from encephalomere VII, have become clearly differentiated in the 3d visceral arch as the *Urvagus* Anlage. Two visceral clefts have appeared.
- Fig. 17. Embryo with 48 somites (7.5 mm.). The fifth and seventh nerves have assumed fibrillar relation with the neural tube. The main branches of the trigeminus begin to appear.



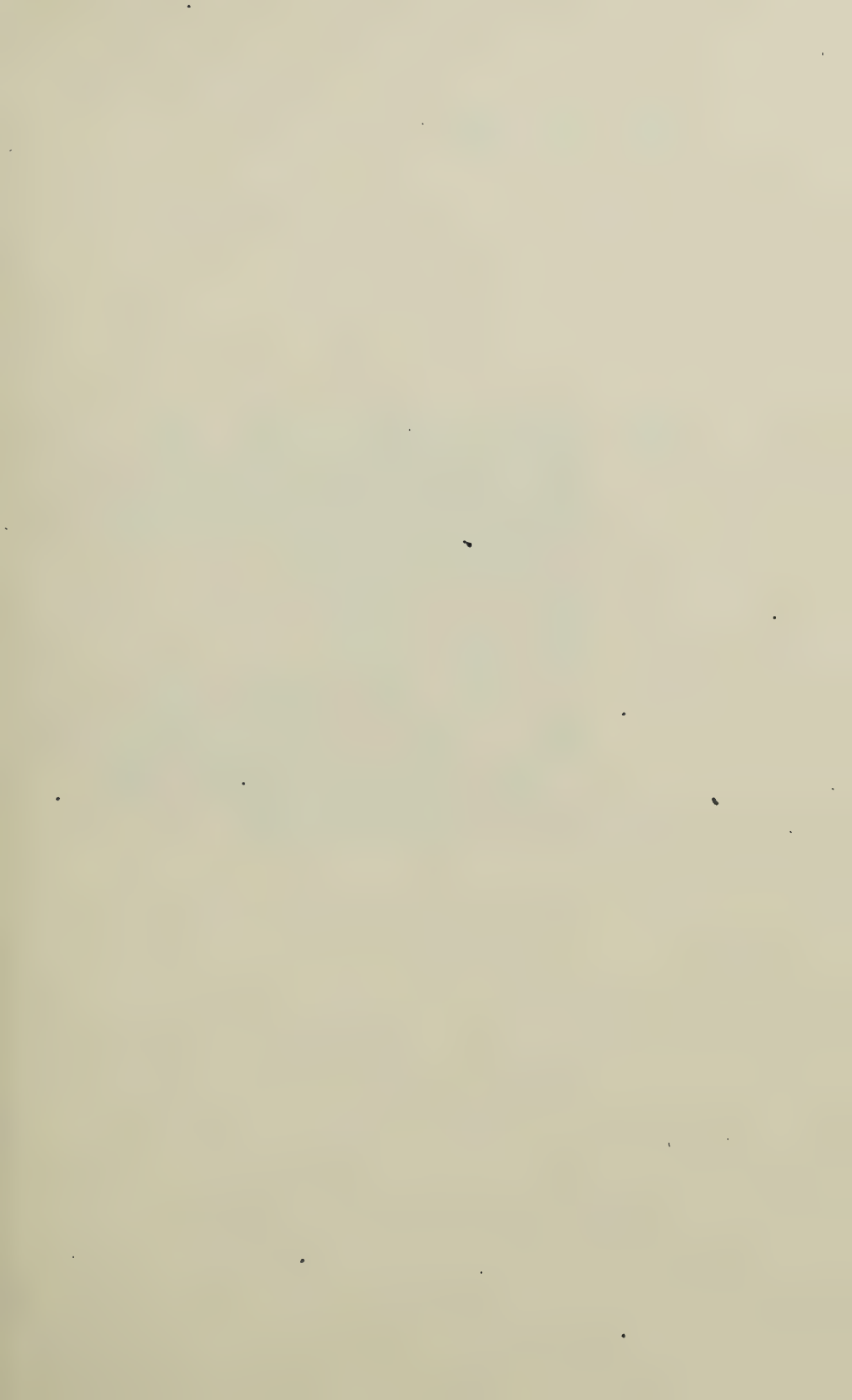
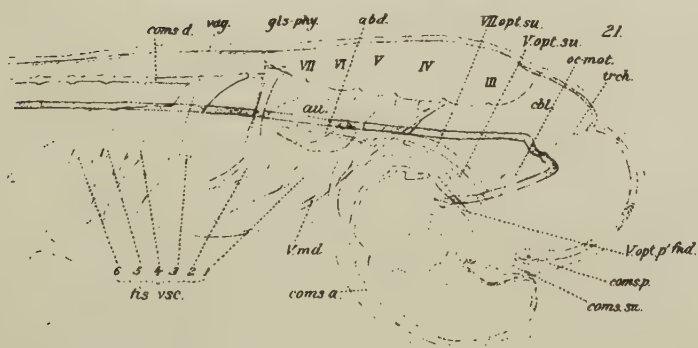
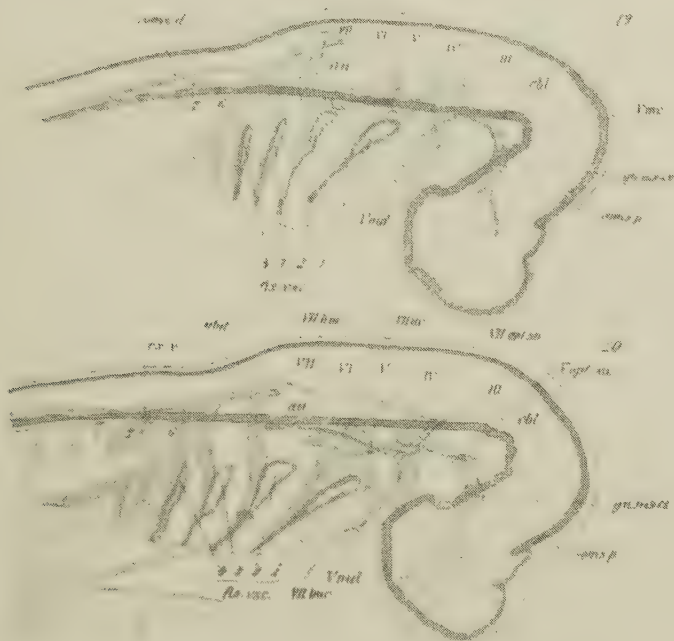
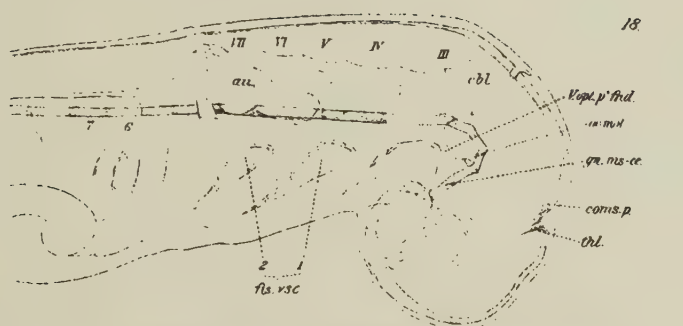


PLATE 4.

Figs. 18 and 21 magnified 28 diameters. Figs. 19 and 20 magnified 21 diameters.

- Fig. 18. An embryo with 52 somites (8 mm.). The otic capsule now lies opposite encephalomere VII. The thalamic and trochlear portions of the trigeminus appear only as scattered clumps of cells. Posterior commissure clearly differentiated. Between this and the preceding stage the oculomotorius has appeared as a fibrillar process from the ventral wall of the midbrain, near *gn. ms-ce.*
- Fig. 19. An embryo with 65 somites (10 mm.). The chief peripheral branches of the cranial nerves have appeared; the abducens, as a process from the ventral wall of encephalomere VII.
- Fig. 20. An embryo with 78 to 80 somites (16 or 17 mm.). In this stage the ramus ophthalmicus superficialis trigemini appears to have fibrillar relation with the mesoderm of the 2d somite, which is growing forward. The fibrous process of the abducens has come into relation with the 3d somite, and also is seen to have a branch passing to the mesoderm posterior to its place of origin. Most of the fibres of the ramus mandibularis trigemini appear in connection with encephalomere III.
- Fig. 21. An embryo 21 or 22 mm. long. The trochlearis is now differentiated, and in relation with the musc. obliquus posterior.



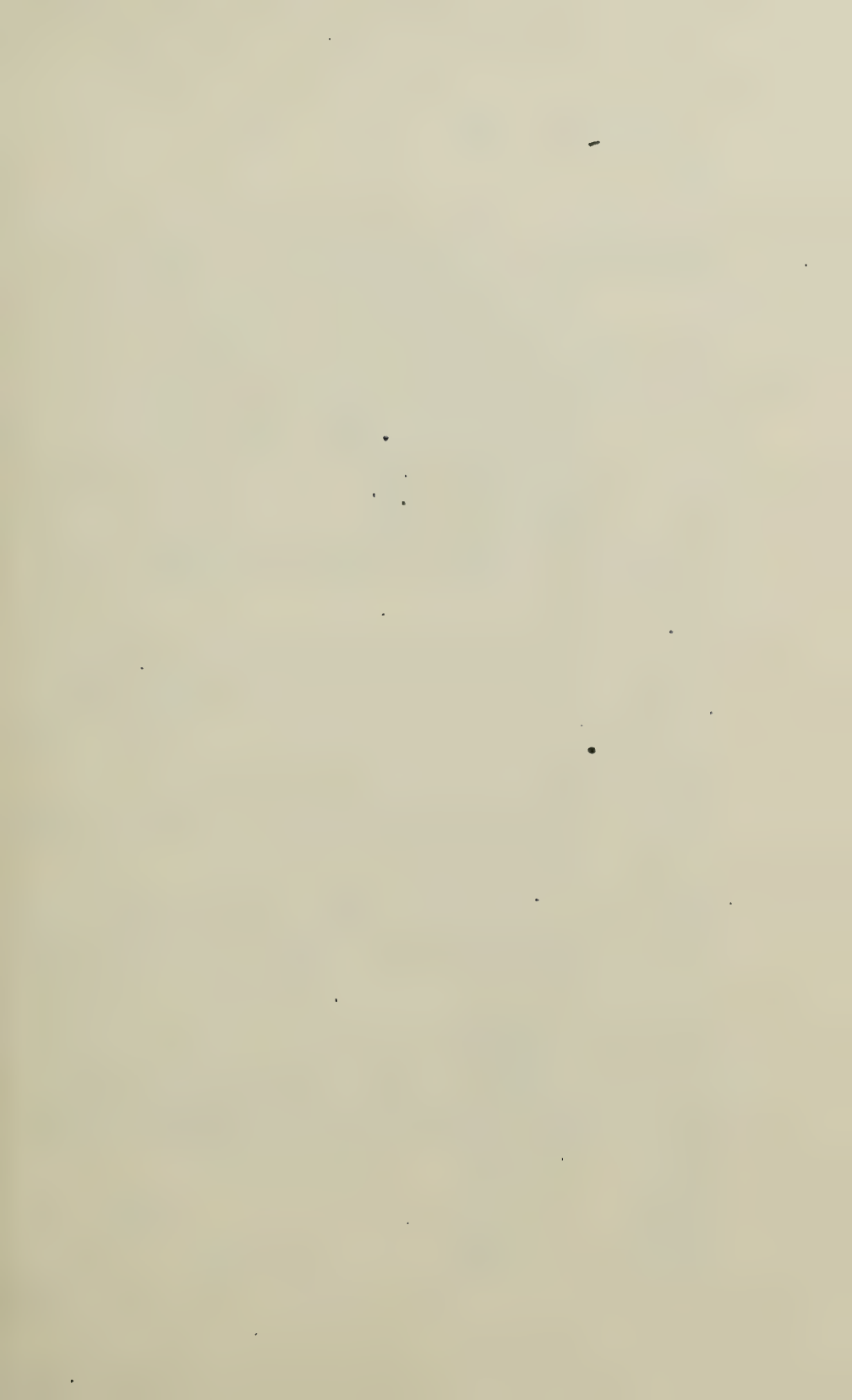


PLATE 5.

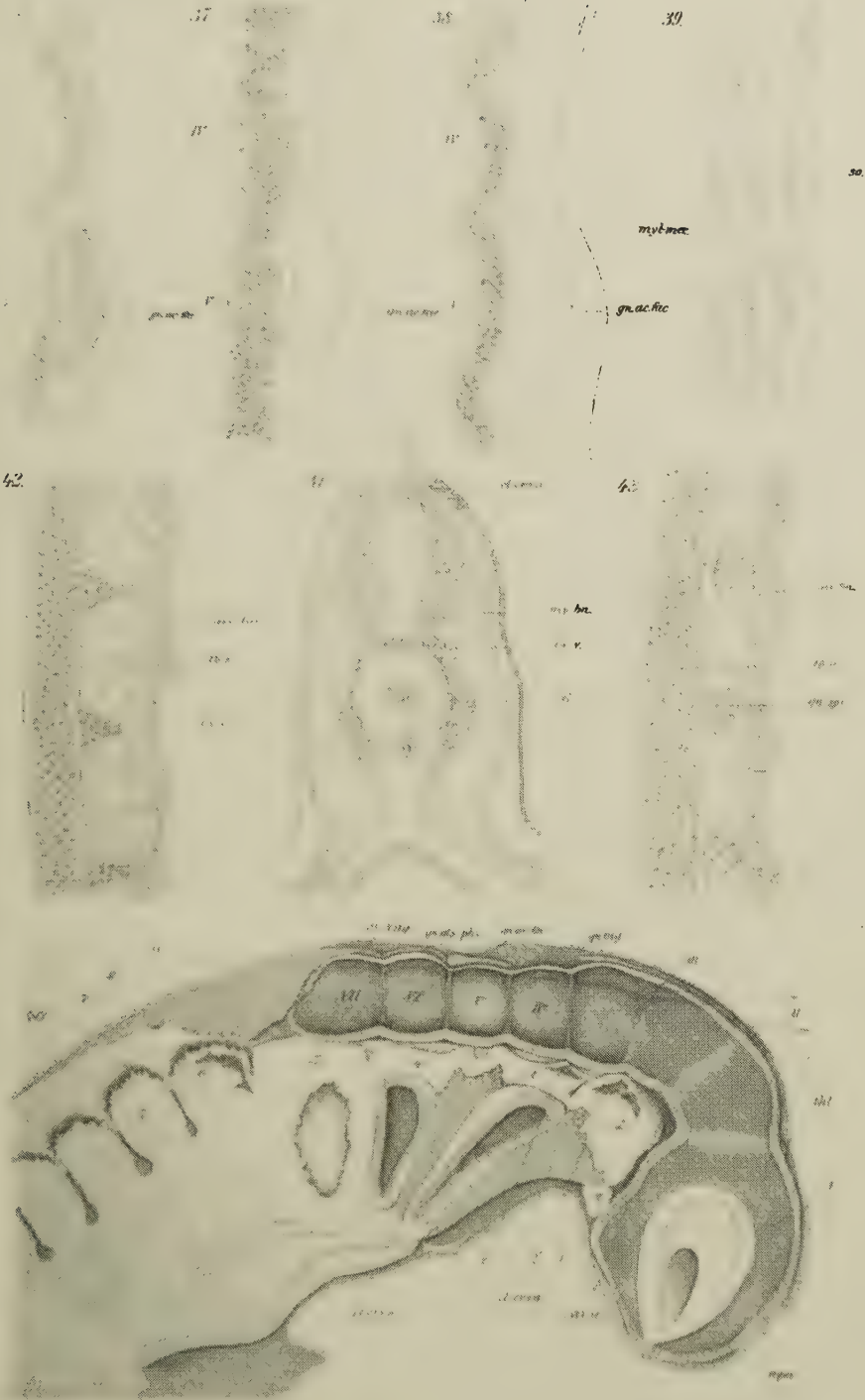
All the Figures except 31 and 32 represent frontal sections of embryos viewed from the dorsal side. All except Figures 25, 32, and 35 are magnified 43 diameters.

- Fig. 22. A frontal section of an embryo with 14 or 15 somites. Encephalomere IV appears as a thickening of the lateral walls of the neural tube. No local thickening seen in the region of encephalomere III.
- Fig. 23. From an embryo with 16 or 17 somites. A local thickening of the lateral walls in the posterior part of encephalomere III appears.
- Fig. 24. From an embryo with 19 or 20 somites. The first four hindbrain neuromeres are now seen as local thickenings of the lateral walls, the thickening of neuromere III affecting its posterior part only.
- Fig. 25. From an embryo with 28 to 30 somites, magnified 75 diameters. Five hindbrain neuromeres are seen. The auditory invagination appears opposite encephalomere VI.
- Fig. 26. From an embryo with 50 somites (8 mm.) in the region of the "Deckplatte," showing the faintly marked expansions of the encephalomeres.
- Fig. 27. A more ventral section of the same embryo. The encephalomeres sharply defined by constrictions. A secondary constriction in encephalomere III appears.
- Fig. 28. A more ventral section of the same series, in the region of the lateral zones. The local thickenings of the encephalomeres well marked.
- Fig. 29. A still more ventral section of the same embryo. The inner cusps between the neuromeres appear as in the more dorsal sections (Fig. 27).
- Fig. 30. Frontal section in the region of the lateral zones of an embryo of 15 mm. The structure of the neuromeres is seen to be the same as that described by Orr ('87) for the Lizard.
- Fig. 31. Cross section of an embryo with 20 somites, in the region of encephalomere IV, to show the thickening of the lateral zones.
- Fig. 32. Cross section of an embryo with 28 to 30 somites in the posterior region of encephalomere III. The lateral zones more markedly thickened than in the previous stage (Fig. 31).
- Fig. 33. Frontal section of an embryo with 50 somites (8 mm.), killed with a mixture of chromic, picric, and sulphuric acids, showing great intensification of the neuromeres, as the result of contraction due to inadequate fixation. The drawing, however, exaggerates the phenomena, since it represents the nuclear regions of the medullary wall with deeper shading.
- Fig. 34. Frontal section of a 19-day *Swine* embryo. The constrictions between the neuromeres are sharply defined.
- Fig. 35. Frontal section of an embryo of *Amblystoma* shortly after the closure of the neural tube. The neural tube is sharply outpocketed in the regions of proliferation of the ganglionic Anlagen of nerves V and VII. No evidence of a thickening or outpocketing comparable with encephalomere IV appears either at this or later stages.

PLATE 6.

All Figures, except 40, magnified 100 diameters. Only the *right* half of the embryo is shown in Figures 36–39, 42, and 44.

- Fig. 36. Frontal section of an embryo with 28 to 30 somites, showing the structure of the neuromeres IV and V in the region of the "Deckplatte."
- Fig. 37. A more ventral frontal section in the same series cut in the region of the lateral zones. The neuromeres appear as well marked local thickenings. The radial arrangement of nuclei much less clearly shown than in the preceding section (Fig. 36).
- Fig. 38. A still more ventral section of the same series, in the region of the "Grundplatte." The inner concavity appears as in the dorsal section (Fig. 36).
- Fig. 39. Frontal section of an embryo with 28 to 30 somites, in the region of the trunk, showing the structure of the myelomeres and their relation to the somites.
- Fig. 40. A reconstruction from sections and dissected specimens of the anterior end of an embryo with 28 to 30 somites, magnified 56 diameters. The lumen of the neural tube is exposed so as to show the hindbrain neuromere as local thickenings of the left wall. Van Wijhe's somites, at this stage separated by clearly marked constrictions, and Platt's anterior somite, are seen. Cells, in chief part derived from the neural crest, are seen surrounding the mesodermic epithelium of the 1st and 2d visceral arches.
- Fig. 41. A cross section of an embryo with 28 to 30 somites in the trunk region. It is seen that the somites press against the ventral half of the neural tube. A migration of mesenchymatous cells from the sclerotome portion of the somite has already begun.
- Fig. 42. Frontal section of an embryo with 50 somites (8 mm.) in the trunk region (ectoderm omitted), taken in the region of the points of exit of the ventral nerves. No constrictions in the ventral wall of the neural tube are to be seen at this stage, but the ventral nerves lie opposite the middle of the somites.
- Fig. 43. A more dorsal frontal section from the same series as Figure 42. Constrictions in the lateral wall, opposite which the ganglia lie, show no corresponding ridges on the inner surface of the lateral wall.



Figures 44 to 53 illustrate the primary and secondary subdivisions of the forebrain and midbrain (encephalomeres I and II). All the Figures, except 47, 48, 53, 55, and 56, magnified 43 diameters.

- Fig. 44. A parasagittal section of a *Chick* embryo of 33 hours' incubation (14 somites). Seven primary expansions of the encephalon appear, from the fifth of which, as in *Squalus*, the Anlage of the acustico-facialis is proliferated.
- Fig. 45. A parasagittal section of a *Squalus* embryo with 18 somites. Six primary vesiculations (encephalomeres) are seen, all included in the region of the cephalic plate. Clefts in the dorsal mesoderm separate from each other all of van Wijhe's somites except the 4th and 5th.
- Fig. 46. A parasagittal section of a *Squalus* embryo with 28 to 30 somites. Both encephalomeres II and III have become subdivided by constrictions, that of the former, however, affecting the ventral wall only. All of van Wijhe's somites separated by clearly marked mesodermic clefts.
- Fig. 47. A parasagittal section of an embryo with 65 somites, magnified 23 diameters. Two subdivisions of encephalomeres I and three subdivisions of encephalomere II appear. The latter remains, however, dorsally a simple expansion. Nerve relation of encephalomeres II and VII with somites 1 and 8 shown.
- Fig. 48. A frontal section in the dorsal part of encephalomeres I and II of an embryo with 30 to 32 somites, magnified 56 diameters. Only two vesiculations appear. Relation of thalamic portion of the trigeminus Anlage to these shown.
- Fig. 49. Frontal section in the dorsal portion of encephalomeres I and II in an embryo with 19 or 20 somites. Two vesiculations only appear.
- Fig. 50. A frontal section of the same embryo as that shown in Figure 48, but more ventral, showing the constriction in the ventral wall of the midbrain.
- Fig. 51. A frontal section of an embryo with 65 somites in the dorsal part of encephalomeres I and II (forebrain and midbrain), showing subdivision (thalamic) of the former.
- Fig. 52. A more ventral frontal section in the same series, showing a constriction in the lateral wall of the midbrain corresponding in position with the posterior commissure (*coms. p.*). The constriction in the forebrain corresponds with the superior commissure.
- Fig. 53. A frontal section, showing forebrain and midbrain regions in an embryo of 22 mm., magnified 23 diameters. Two constrictions only appear, one in the region of the superior commissure, and the other in the region of the posterior commissure.
- Fig. 54. A cross section of an embryo with 6 or 7 somites in the region of the cephalic plate, showing the ventral flexure of its edges.
- Fig. 55. A cross section of an embryo at a stage when the edges of the neural plate are about to be raised, showing the differentiation of a neural crest in the anterior part of the cephalic plate. Magnified 100 diameters.
- Fig. 56. A cross section in the posterior part of the cephalic plate of an embryo with 9 or 10 somites, showing that migration of neural-crest cells has already begun. Magnified 85 diameters.

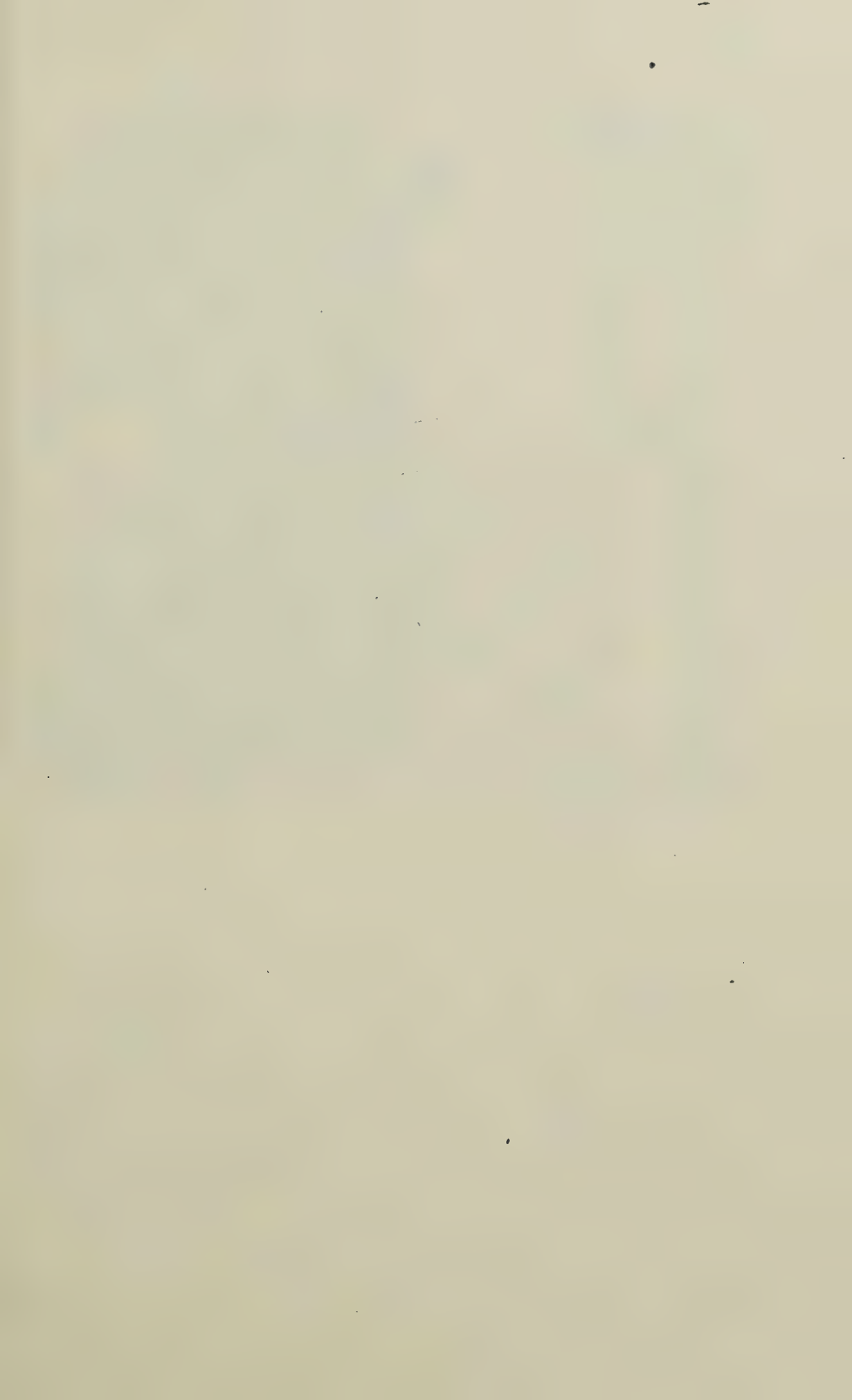
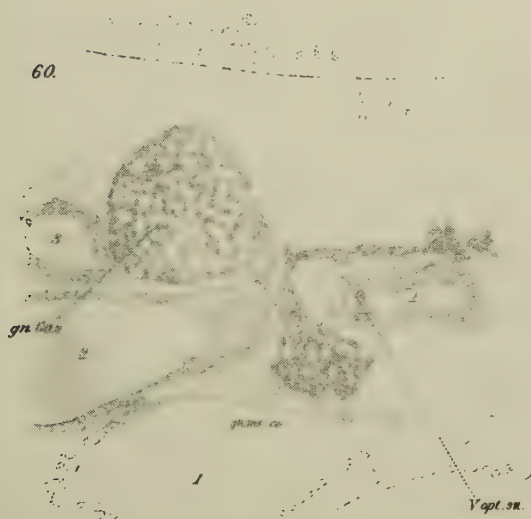
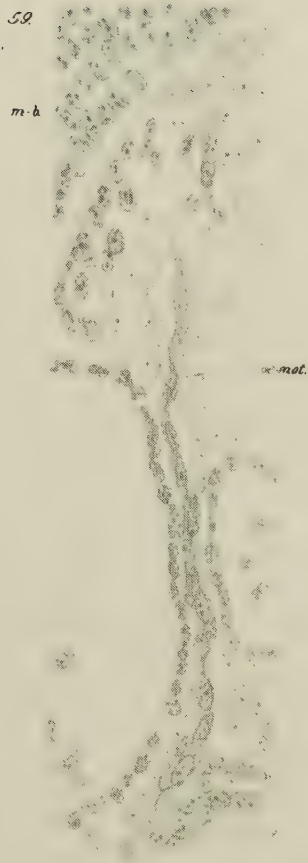
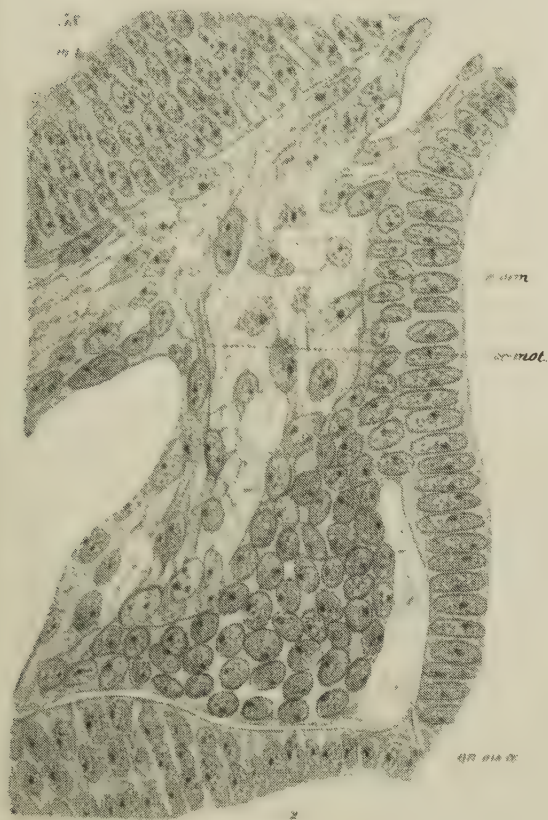
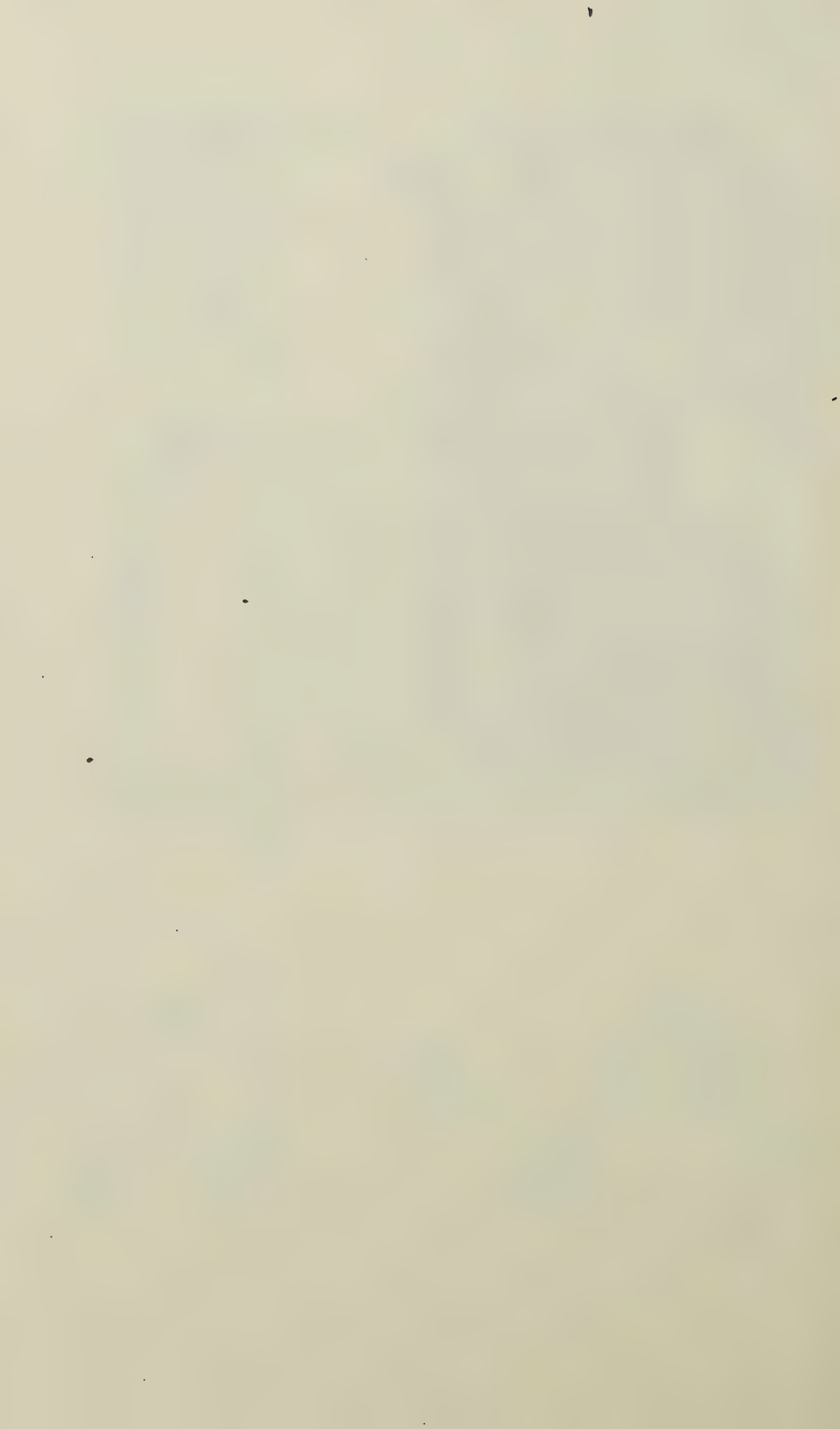


PLATE 8.

Stages in the development of the nerves oculomotorius, ramus ophthalmicus superficialis trigemini, and ramus ophthalmicus profundus trigemini.

- Fig. 58. A frontal section of an embryo with 55 somites (8½–9 mm.). Embryo killed with Davidoff's fluid. The oculomotorius appears as a cellular strand extending from the inner side of the mesocephalic (profundus) ganglion to the wall of the midbrain. Magnified 500 diameters. Reconstructed from three sections.
- Fig. 59. A sagittal section of an embryo with 56 somites. Embryo killed with Davidoff's fluid. Near the brain the nerve appears composed of loose fibrillæ, while peripherally it is cellular in appearance. Magnified 360 diameters. Reconstructed from five sections.
- Fig. 60. A combination of two parasagittal sections through the left side of an embryo of 16 mm. Protoplasmic processes from the ramus ophth. sup. trig. appear in relation with the anterior projection of the 2d cavity (muscul. obl. superior). Magnified 70 diameters.
- Fig. 61. A parasagittal section from the right side of an embryo with 51 or 52 somites (8 mm.). A well marked fibril passes from the mesocephalic ganglion to van Wijhe's 1st somite. The oculomotorius has not yet appeared.





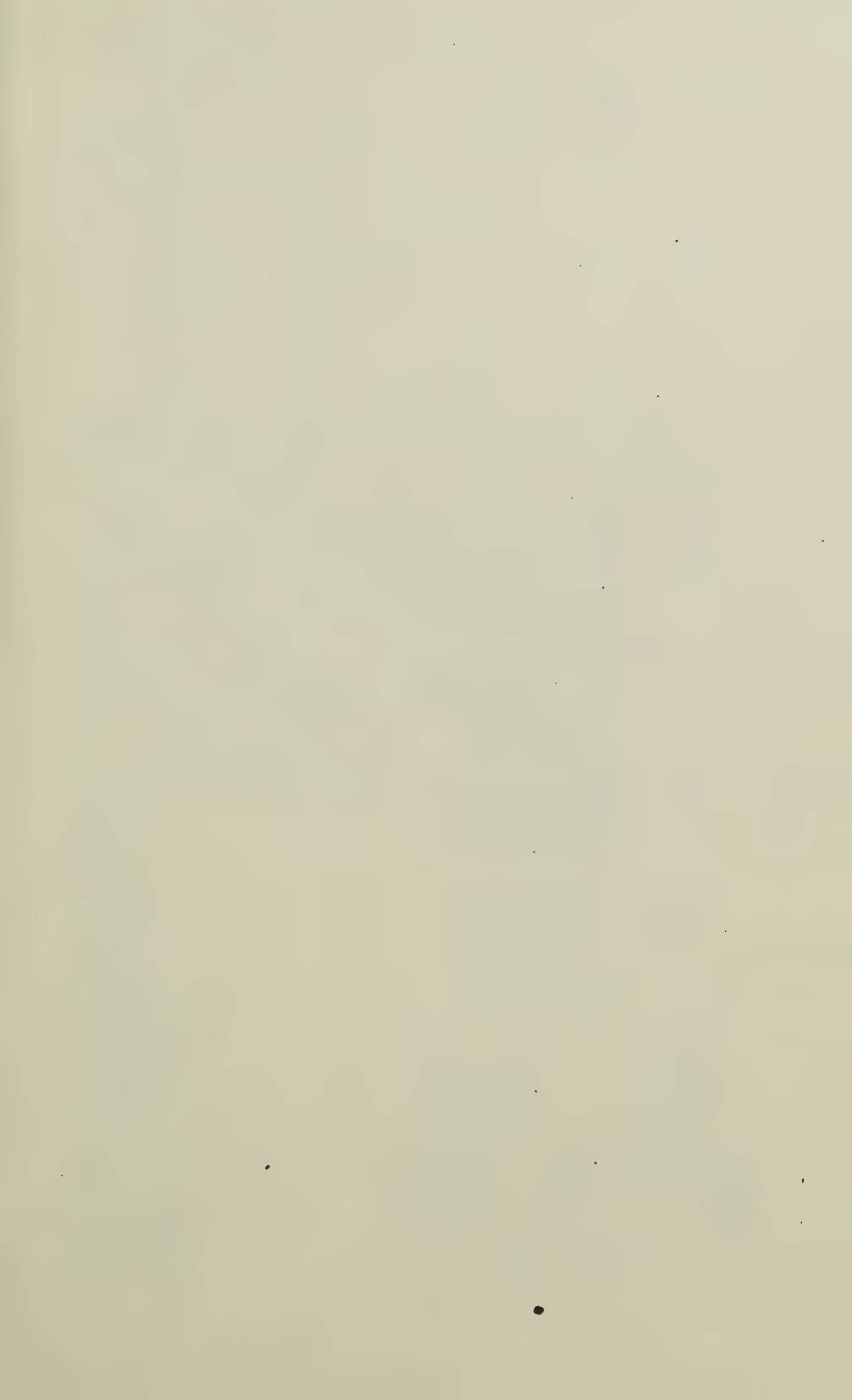
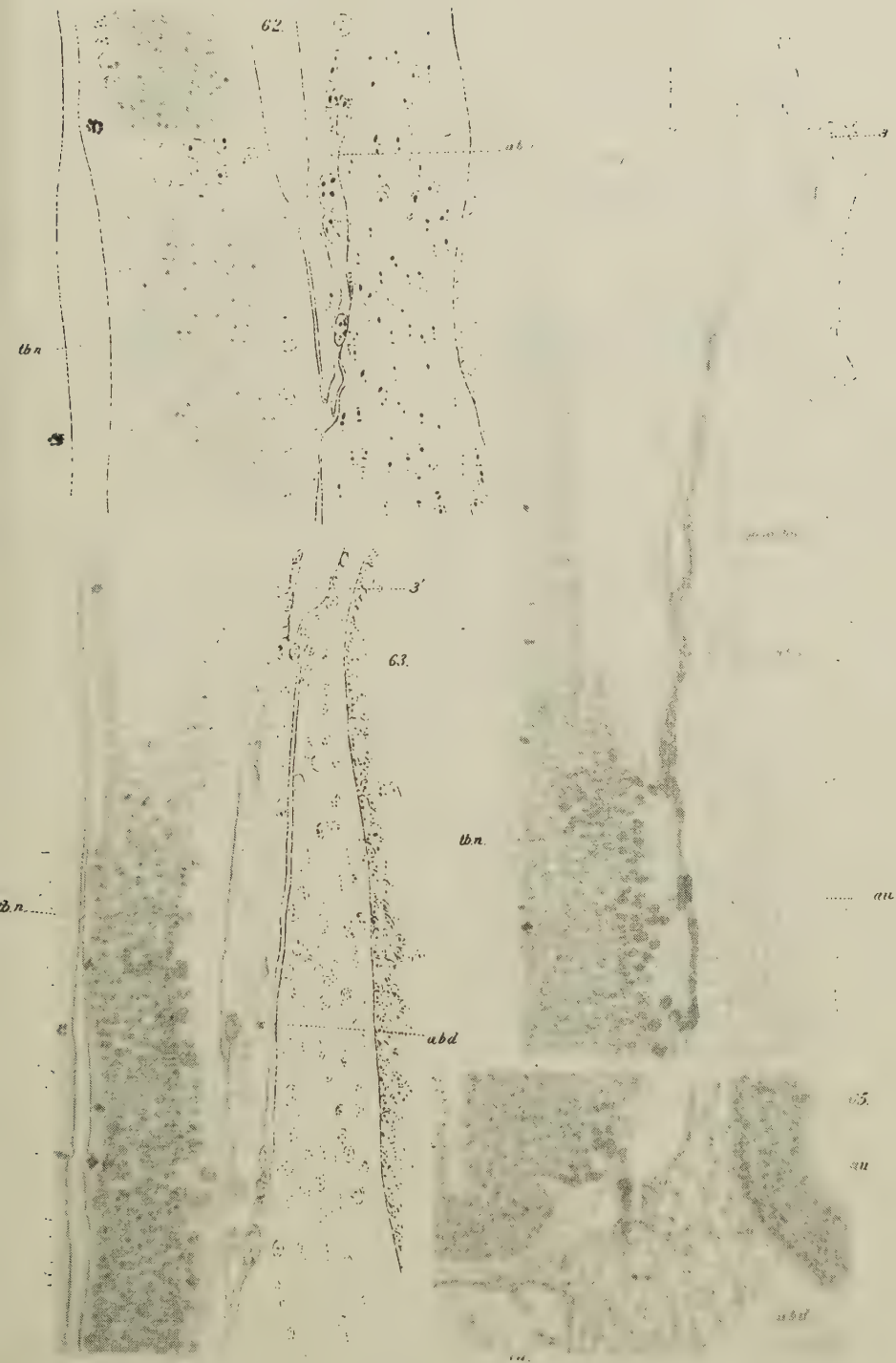
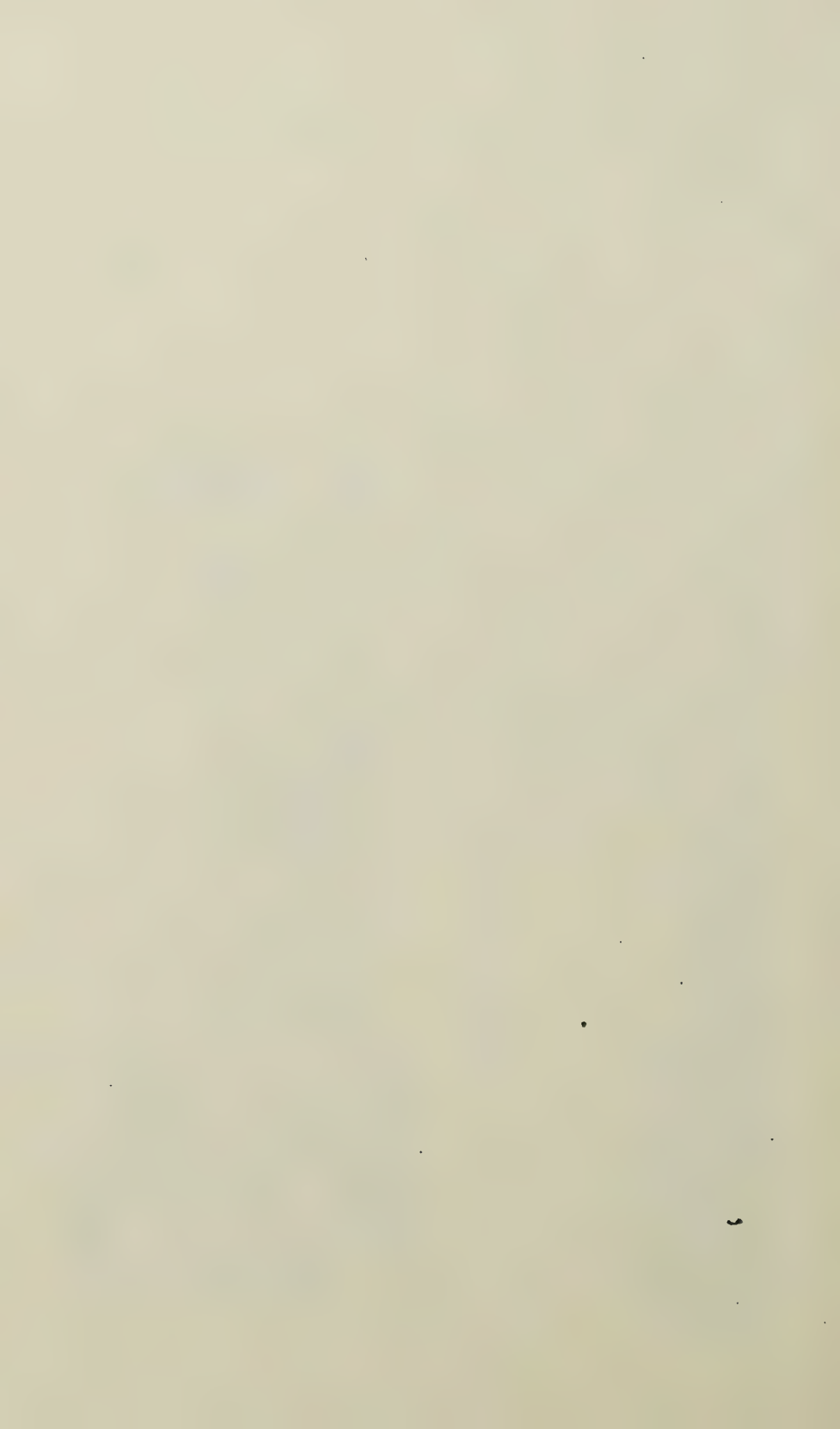


PLATE 9.

Stages in the development of the abducens nerve. All the specimens were killed with Davidoff's fluid (corrosive-acetic). All Figures are from frontal sections except Figure 65.

- Fig. 62. A frontal section of an embryo with 62 somites (9 mm.). Magnified 450 diameters. Two roots are present.
- Fig. 63. From an embryo with 68 somites (10 mm.) magnified 285 diameters. The course of the nerve is very direct in this stage, at least in the specimen figured. Throughout the most of its course it is entirely free from nuclei.
- Fig. 64. A combination from 7 sections of an embryo with 80 somites. Three roots present on the side of the embryo figured. Deeply staining nuclei appear in close connection with the nerve, and there is some (in my opinion doubtful) evidence of the migration of nuclei to or from the neural tube. Peripherally the nerve divides into fine fibrillæ. Magnified 200 diameters.
- Fig. 65. A cross section of an embryo with 75 somites in the region of the posterior root of the abducens, magnified 285 diameters. Evidence of migration of nuclei (?).





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Reports on the Results of Dredging Operations in 1877, 1878, 1879, and 1880, in charge of ALEX-
ANDER AGASSIZ, by the U. S. Coast Survey Steamer "Blake," as follows:—

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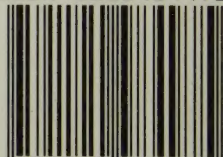
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